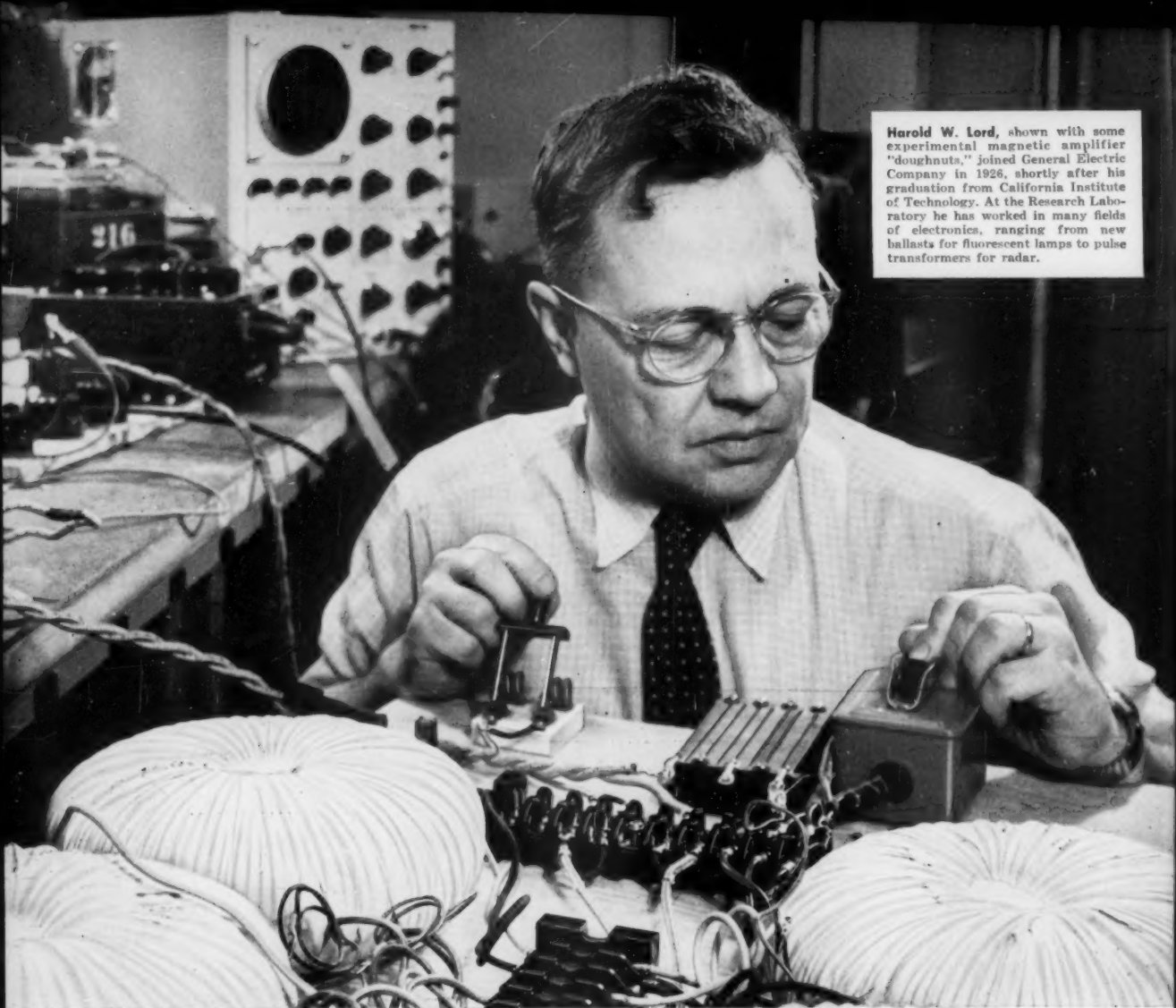


# SCIENCE

1 June 1956

Volume 123, Number 3205

<b>Editorial</b>	Emphasis on Mathematics .....	965
<b>Articles</b>	Trail of Sulfur Research: from Insulin to Oxytocin: <i>V. du Vigneaud</i> ....	967
	Charles C. Adams, Ecologist: <i>P. B. Sears</i> .....	974
	E. R. Dunn, Herpetologist: <i>R. Conant</i> .....	975
<b>News of Science</b>	Meteorology and Atomic Energy; Junior Academies of Science; Socio-Psychological Prize Judges; Civil Service Science Salaries; AEC Headquarters; New Canadian Clinics; Heart Disease Mortality in Women; Pygmies in New Guinea; News Briefs; Scientists in the News; Recent Deaths; Education; In the Laboratories .....	976
<b>Reports and Letters</b>	New Color Test for Thiols and Thioesters: <i>R. Benesch et al.</i> .....	981
	Radioactivity in Thyroid Glands Following Nuclear Weapons Tests: <i>L. Van Middlesworth</i> .....	982
	Gum Replica Technique for Electron or Light Microscopy: <i>G. E. Hess and E. J. Schantz</i> .....	983
	Action of <i>p</i> -(Di(2-chloroethyl))-amino-L-phenylalanine of Harding-Passey Mouse Melanoma: <i>J. M. Luck</i> .....	984
	Increased Frequency of Births in the Morning Hours: <i>P. D. King</i> .....	985
	Adrenal Cortex and the Parotid Secretion of Sodium-Depleted Sheep: <i>J. R. Goding and D. A. Denton</i> .....	986
	Cholinesterase Activity of Human Leucocytes: <i>G. H. Denny, Jr., and D. D. Hagerman</i> .....	987
	Clinical Experiment on the Use of Sodium N-Lauroyl Sarcosinate in the Control of Dental Caries: <i>L. S. Fosdick</i> .....	988
	Demonstration of Particulate Adhesion of the Rieckenberg Type with the Spirochete of Syphilis: <i>C. Lamanna and D. H. Hollander</i> .....	989
	Duttonite, New Vanadium Mineral from Peanut Mine, Montrose County, Colorado: <i>M. E. Thompson, C. H. Roach, R. Meyrowitz</i> .....	990
	Lack of Recognition of Foreign Works: <i>R. C. Mitchell</i> .....	990
	Serum Protein Concentrations in the North American Negroid: <i>H. M. Rawsley, V. L. Yonan, J. G. Reinhold</i> .....	991
	Green Crabs and the Redistribution of Quahogs: <i>J. M. Moulton and A. H. Gustafson</i> .....	992
	Serotonin-Releasing Activity Limited to <i>Rauwolfia</i> Alkaloids with Tranquilizing Action: <i>B. A. Brodie, P. A. Shore, A. Pletscher</i> .....	992
<b>Book Reviews</b>	<i>Reflections of a Physicist; Physiologie der Zelle; Ergebnisse der Medizinischen Grundlagenforschung; International Review of Cytology; Yearbook of Anthropology, 1955; Books Reviewed in The Scientific Monthly, June; New Books; Miscellaneous Publications</i> .....	994
<b>Scientific Meetings</b>	Cosmic-Ray Colloquium; Meeting Notes; Society Elections; Forthcoming Events .....	997
	Equipment News .....	1002



Harold W. Lord, shown with some experimental magnetic amplifier "doughnuts," joined General Electric Company in 1926, shortly after his graduation from California Institute of Technology. At the Research Laboratory he has worked in many fields of electronics, ranging from new ballasts for fluorescent lamps to pulse transformers for radar.

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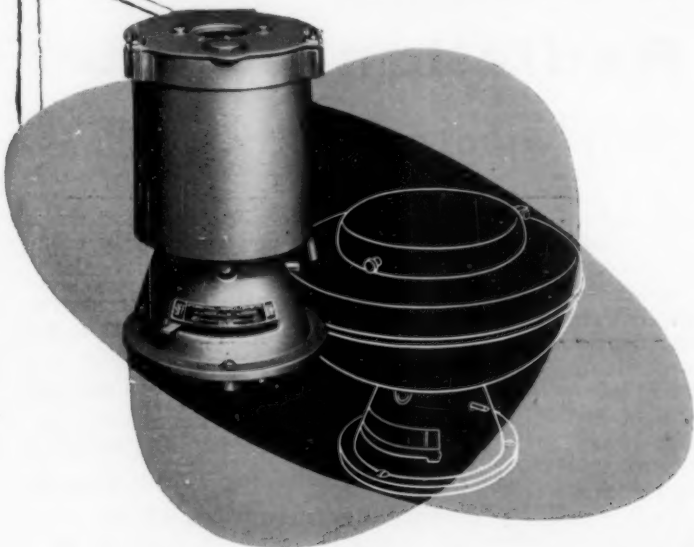
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SCIENCE founded in 1880, is published each Friday by the American Association for the Advancement of Science at Business Press, Lancaster, Pa. Entered at the Lancaster, Pa., Post Office as second class matter under the Act of 3 March 1879.

SCIENCE is indexed in the *Reader's Guide to Periodical Literature* and in the *Industrial Arts Index*.

Editorial and personnel-placement correspondence should be addressed to SCIENCE, 1515 Massachusetts Ave., NW, Washington 5, D.C. Manuscripts should be typed with double spacing and submitted in duplicate. The AAAS assumes no responsibility for the safety of manuscripts or for the opinions expressed by contributors. For detailed suggestions on the preparation of manuscripts, book reviews, and illustrations, see *Science* 123, 714 (27 Apr. 1956).

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## Emphasis on Mathematics

If college teachers of science could select the area of science in which they would most like to have their entering students show proficiency, mathematics would undoubtedly be first choice. No other discipline—except language itself—is so fundamental to all of science and of such widespread usefulness to scientist and nonscientist alike.

Despite the importance of mathematics, instruction is suffering from several ailments. Much of the curriculum, from arithmetic to the calculus or beyond, is out of date. The typical youngster is introduced to arithmetic by a teacher with little knowledge of, or interest in, this subject. At the high-school level there is a shortage of well-qualified teachers, and there has been a declining emphasis on rigorous mathematical work. College time is being devoted to remedial courses in algebra and geometry, and sometimes even in arithmetic. As a result of these ailments, some students learn little and others learn things of little use. The fifth-grader still has to learn that there are 320 rods in a mile. Despite the everyday usefulness of concepts of probability, few students get far enough to be introduced to this subject. Social science majors find much of the traditional material irrelevant. Even the mathematics major has to wait a long time before he gets into modern mathematics. Throughout the school years, mathematics ranks low in popularity, but former students of all levels rank it high when asked: In which subjects do you wish you had had more work?

Mathematicians are attempting to improve the situation, but their efforts are not enough. The problem is broad enough to make it a general scientific and educational responsibility. Perhaps we should dramatize the general importance of mathematics and bring pressure on the schools to give better instruction to more students.

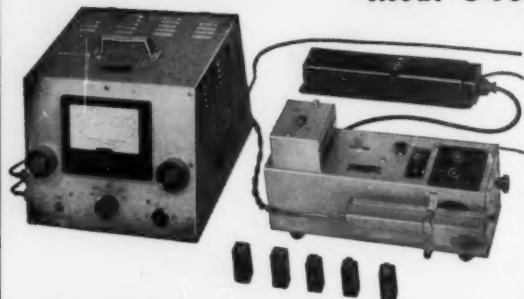
Higher college entrance requirements in mathematics—or in English or other subjects basic to good preparation for college work—will put pressure on high schools to improve their instruction. Pressure from above is not the only, or even the most desirable, method of improving high-school programs. But pressure from colleges is a wholly legitimate method of strengthening the education of the growing fraction of high-school students who are planning to enter college.

I. I. Rabi recently suggested a more ingenious method of emphasizing mathematics. Rabi proposed to the Joint Congressional Committee on Atomic Energy that winners of federal scholarships be selected by an examination in mathematics; any high-school graduate who passed with satisfactory marks an examination over a 4-year program of mathematics would be entitled to a college scholarship for his freshman year, and any freshman who passed an examination in the calculus (or higher course if the calculus was taken in high school) would have his fellowship renewed.

The details have not been worked out, but the purpose is clear: to emphasize the importance of acquiring a good mathematical foundation. Students given these scholarships would be free to choose whatever fields of specialization each preferred, for the purpose would be to insure that a larger number of students secured the mathematical foundation that would be valuable whether they chose to become scientists, economists, engineers, or businessmen.

Whether or not these suggestions represent the best means of accomplishing this end, it is time to put very special emphasis on the importance of mathematics.—D. W.

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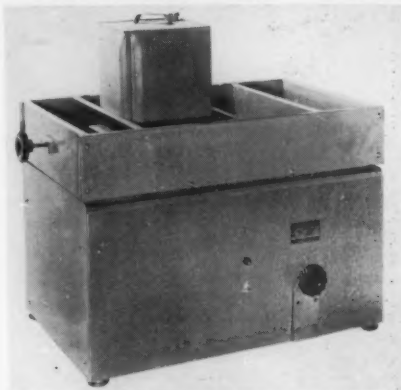
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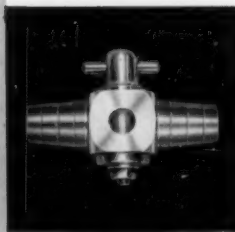
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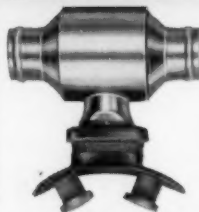
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## Trail of Sulfur Research: from Insulin to Oxytocin

Vincent du Vigneaud

The work on biochemically important sulfur compounds, cited in the Nobel award, formed a part of a trail of "sulfur research" that began approximately 30 years ago with a study of the sulfur of insulin and encompassed recently the first synthesis of a polypeptide hormone. The latter sulfur-containing hormone, oxytocin, is the principal uterine-contracting and milk-ejecting hormone of the posterior pituitary gland. It might therefore be of interest to unravel some of the stepwise evolution of our researches from insulin to oxytocin and to bring into focus the background of the research findings and the thinking behind the researches.

I have had the pleasure of following this trail of research in the company of a group of graduate students and postdoctoral associates, without whose loyal and effective collaboration the trail that I am going to describe could not have been worked out.

This trail becomes apparent only in retrospect. Obviously, I did not start out to study sulfur as my life's work. And yet, as I look back over the trail of many years, I encounter the fact that this thread of sulfur has been the thread of continuity running through practically all of my research endeavors.

I find it intriguing to contemplate how one starts out on a trail of exploration in the laboratory, not knowing where one is eventually going—starting out, to be sure, with some immediate objective in mind but also having a vague sense of

something beyond the immediate objective toward which one is striving. The thrill of this kind of research, albeit at a sublimated level, is analogous, I am sure, to the thrill that explorers like the Vikings of old experienced in breaking through the confines of the known world.

As one looks back on a trail of research, one sees that the continuity is sometimes greater than he may have imagined at the time. As I look back, it seems almost inevitable that I should have proceeded from the pancreatic hormone, insulin, to the posterior pituitary hormone, oxytocin, via sulfur. Again, in looking back, I now realize that there were times when we stopped to work out more fully the chemistry of other sulfur-containing compounds, such as cystine, homocystine, and methionine, and to study their metabolic significance in transsulfuration and transmethylation. These researches diverted us into interesting bypaths. However, strangely enough, as I shall try to bring out, many of these experiences, particularly the cystine peptide work and the knowledge of certain reactions involving sodium and liquid ammonia that we gained along the route, were vital when we came to study the posterior pituitary hormones.

### Insulin

Where did the sulfur trail start? I think it started at the University of Illinois, where my first teacher in biochemistry was the late H. B. Lewis, who was extremely enthusiastic about sulfur. It was his enthusiasm that undoubtedly aroused my interest in the biochemistry of sulfur compounds.

In my work in organic chemistry at

that same university with C. S. Marvel, I developed a strong interest in the relationship of organic chemical structure to biological activity. The continuing interest in this relationship has also influenced greatly the direction of this trail of research. The work I did with Marvel was concerned with the synthesis of compounds which we hoped would have a local anesthetic effect accompanied by an epinephrinelike effect. As I look back over the trail, I find this theme—the relation between biological activity and organic chemical structure—recurring again and again.

My interest in insulin was initiated through a lecture given by W. C. Rose, who succeeded Lewis as professor of biochemistry at Illinois. On his return from a meeting in Toronto in 1923, he gave an account of the exciting discovery of insulin by Banting and Best. I well recall the thrill of listening to Rose and my curiosity about the chemical nature of a compound that could bring about the miracles he described. Little did I know at that time that insulin would eventually turn out to be a sulfur compound.

Some 2 years later, I received an invitation from J. R. Murlin at the University of Rochester Medical School to come and work on the chemistry of insulin in his department, a department that was devoted mainly to endocrinology and metabolism. The chance to work on the chemistry of insulin transcended all other interests for me, and I accepted Murlin's invitation.

While I was at Rochester, I became intrigued with the fact that all of our preparations contained sulfur, and most of my efforts during the next 2 years were devoted to studying the sulfur of these insulin preparations. From these studies, I came to the conclusion that the sulfur was present in the form of the disulfide linkage and that insulin was most likely a derivative of the amino acid, cystine, and the suggestion was made that the cystine in insulin was linked to the rest of the molecule by peptide linkages (1).

The following year, while working in Abel's laboratory at Johns Hopkins University, I took up the isolation of cystine from crystalline insulin, because the conclusive proof of the presence of cystine in insulin had to rest on the isolation of cystine in pure form. This isolation was eventually accomplished (2). As I con-

Dr. du Vigneaud is professor of biochemistry at Cornell University Medical College. This article is based on a lecture that he gave 12 Dec. 1955, when he was awarded the Nobel prize in chemistry for 1955. It is published here with the permission of the Nobel Foundation.

tinued work at Johns Hopkins on insulin in collaboration with Jensen and Wintersteiner, we could find nothing but ordinary amino acids and ammonia in acid hydrolyzates of insulin (3, 4).

The presence of cystine in insulin naturally brought many questions to mind. One of the first questions that occurred to me was whether various combinations of cystine with other amino acids in peptide linkage might affect the lowering of blood sugar. It was then realized that as yet no peptide of cystine that was linked through the carboxyl group of cystine had been prepared. No method was available at the time for the synthesis of this type of peptide. Therefore, while the researches on insulin were continued over the next several years, parallel studies were carried out with several graduate students on the synthesis of peptides of cystine.

### Cystine Peptides

Although the peptides we eventually made did not have hypoglycemic activity, the work we did on them gave us valuable experience in the synthesis of cystine peptides and also led to a synthesis of the biologically important compound, glutathione, a tripeptide of glutamic acid, cysteine, and glycine. This work on cystine peptides led to the development by us of several reactions involving sodium and liquid ammonia, which, almost 20 years later, played a vital role in our synthesis of oxytocin. One of these reactions was the removal of a carbobenzoxy group by sodium in liquid ammonia, and another was the utilization of a benzyl group to cover the sulfur of cysteine during certain steps of synthesis and its final removal by means of sodium in liquid ammonia.

As is well known, Bergmann and

Zervas introduced in 1932 the now classical method of protecting an amino group during the course of peptide synthesis with what they called a carbobenzoxy group (5). Their procedure led to the carbobenzoxy derivative of the peptide, and the carbobenzoxy group was removed by catalytic reduction with hydrogen. However, their procedure did not lend itself to the preparation of cysteine or cystine peptides.

Two years after the appearance of the Bergmann-Zervas method, it occurred to me that the carbobenzoxy group might possibly be cleaved from the amino group of cystine by reduction with sodium in liquid ammonia. If so, a convenient method for the synthesis of cystine peptides might result. In work with Audrieth and Loring (6), we had already prepared cysteine from cystine by this method of reduction.

The reduction of dicarbobenzoxy-cystine was therefore attempted in work with Sifferd (7). The compound was dissolved in liquid ammonia, and sodium was added until a permanent blue color was obtained. After evaporation of the ammonia and subsequent oxidation of the cysteine by aeration of the slightly alkaline solution, cystine was obtained in almost quantitative yield.

In our earlier work on the preparation of cysteine, it had occurred to us that it might be possible to benzylate the sulfhydryl group of cysteine by adding benzyl chloride to the liquid ammonia solution of the sodium salt of cysteine produced by the reduction of cystine with metallic sodium. An excellent yield of S-benzylcysteine was obtained. Although the latter reaction was carried out in 1930 with Loring and Audrieth, it was not until sometime later that the possibility of cleaving a benzyl thio ether by this same means occurred to us in our work with Sifferd. S-Benzylcysteine was cleaved to

cysteine in liquid ammonia with metallic sodium, cystine being isolated after oxidation (7).

This same reductive procedure was also applied to the preparation of cystinylbisglycine from dicarbobenzoxy-cystinylbisglycine and of cysteinylglycine from S-benzylcysteinylglycine (8).

### Glutathione

The effectiveness of these reactions impressed us with their potentialities as possible key reactions for a synthesis of glutathione, the structure of which was believed, through the work of Hopkins (9) and of Kendall, Mason, and McKenzie (10) to be  $\gamma$ -L-glutamyl-L-cysteinylglycine. If we could synthesize N-carboboxy- $\gamma$ -glutamyl-S-benzylcysteinylglycine, we felt that its reduction with sodium in liquid ammonia should yield glutathione.

This approach to glutathione would have a particular advantage in that the sulfhydryl group would be covered by a benzyl radical up to the final step, and thus, during the course of the various reactions that might be employed up to this point, the likelihood of partial oxidation of the sulfhydryl group and its attendant difficulties would be eliminated.

In work with Miller (11), we were able to obtain this desired intermediate by the coupling of suitable derivatives of the three amino acids involved. As is shown in Fig. 1, reduction of this intermediate with sodium in liquid ammonia gave glutathione, which, upon isolation in crystalline form, was shown to be identical with the natural product. Our synthesis followed shortly after the first synthesis of glutathione by Harington and Mead by a somewhat different approach (12).

While this synthesis was going on, we continued our work on insulin, mainly along two lines. The first was concerned with determining whether the cystine content accounted for all of the sulfur; and the second, with the behavior of insulin upon reduction of the disulfide groups. After some 7 years of work, we finally were able to account for the sulfur of insulin entirely on the basis of cystine (13), and we could obtain no evidence for any sulfur compound other than cystine in insulin (14, 15).

The study of the reduction of insulin led directly to our work on the posterior pituitary hormones. With such a gentle reducing agent as cysteine or glutathione acting at room temperature and at a neutral pH, insulin became inactivated, reduction of the disulfide linkages being undoubtedly the cause of the inactivation (16-18). Reoxidation did not restore activity.

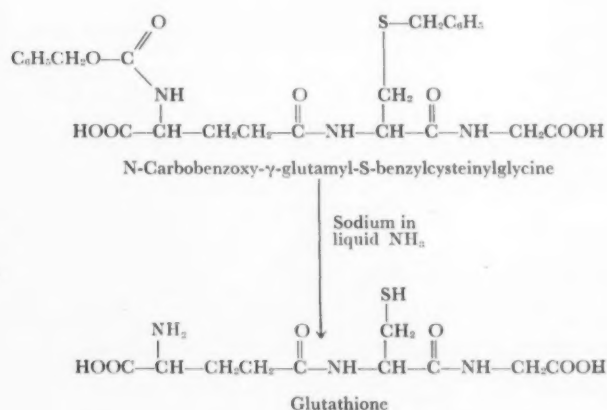


Fig. 1. A synthesis of glutathione.

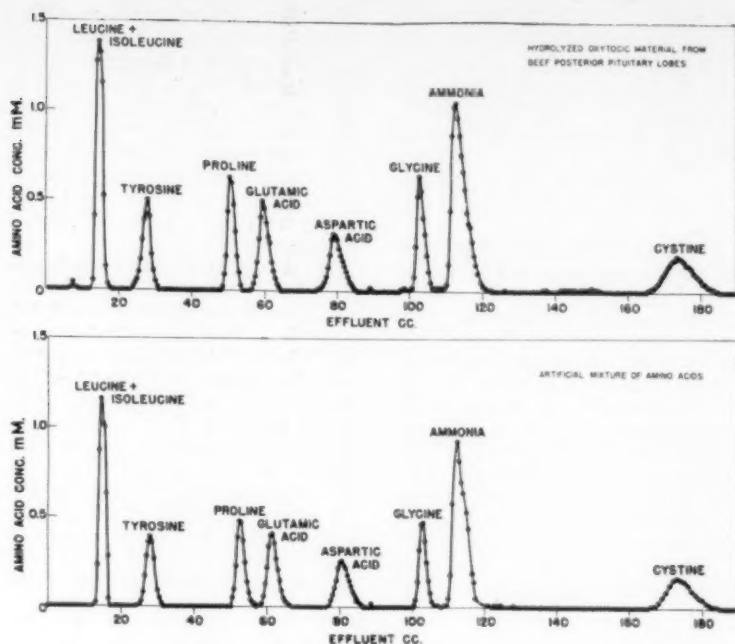


Fig. 2. Separation of amino acids from a hydrolyzate of oxytocin (upper chromatogram) and from an artificial mixture of amino acids simulating the composition of oxytocin (lower chromatogram). Solvents, 1:2:1 *n*-butyl alcohol-*n*-propyl alcohol-0.1N HCl followed by 2:1 *n*-propyl alcohol-0.5N HCl.

### Posterior Pituitary Hormones

The work on insulin aroused our interest in other protein or proteinlike hormones. We turned to the examination of oxytocin, the uterine-contracting hormone, and vasopressin, the blood-pressure-raising hormone, of the posterior pituitary gland. There were some indications in the literature that these hormones might be polypeptidelike substances of lower molecular weight than insulin. Furthermore, there was evidence that partially purified preparations of these hormones contained sulfur, but the nature of the sulfur was unknown. We thought it would be interesting to investigate these hormones in comparison with insulin, and in 1932 we made some preliminary explorations on these hormones. In this discussion I will confine my attention mainly to oxytocin, with only occasional reference to vasopressin.

Kamm and Grote of Parke, Davis and Company kindly placed at our disposal some of their partially purified oxytocin, and we were able to show that, upon hydrolysis, the samples contained approximately 9 percent cystine (19). Of course, we could not tell at that time whether the cystine was present in the hormone or in the impurities. Nevertheless, in the work with Sealock (20), we decided to treat the partially purified oxytocin with cysteine and find out

whether this hormone lost its activity like insulin. Much to our surprise, the oxytocic activity remained. Oxidation, by aeration of an aqueous solution until the sulfhydryl test was negative, did not cause loss of activity. The question then occurred: Had we really reduced the hormone by the cysteine treatment? It appeared possible to us that if the hormone were a disulfide and had been reduced, treatment with benzyl chloride might cover the sulfhydryl group with a benzyl radical and inactivation might take place. When the reduced oxytocin preparation was treated with benzyl chloride, inactivation did result. On the other hand, treatment of the nonreduced material with benzyl chloride did not cause inactivation. These results made us fairly certain that the oxytocic principle contained sulfur in the form of a disulfide linkage (20).

We also investigated the behavior of the vasopressin preparation on cysteine treatment and found it quite parallel to that of the oxytocin preparation. This aroused in us the desire to see what the pure compounds themselves would be like. What manner of compounds were they? Were they, like insulin, also simply made up of amino acids and ammonia? Since we had reason to believe that they were smaller molecules than insulin, it seemed to me that they might lend themselves to an organic chemical approach.

If we could isolate them, we thought we might be able to work out their structure and perhaps synthesize them.

### Isolation

The purification was a slow process, for the amount of active principles in the gland is extremely small, the principles are unstable, and the bioassays involved are very time-consuming. Hundreds of thousands of hog and beef glands were used during the course of the investigations. Up to the time of World War II, we made considerable progress in collaboration with Sealock, Irving, Dyer, and Cohn on the purification of the principles, mainly through electrophoretic techniques, and learned much about the behavior of the hormones (21-26).

We laid aside the problem during the war for certain assignments, particularly on penicillin, but thereafter the isolation of oxytocin was undertaken in collaboration with Livermore (27). Since the countercurrent distribution technique developed by Craig (28) for the purification of organic compounds had played a helpful role in our isolation of synthetic penicillin, we naturally thought of using countercurrent distribution on partially purified oxytocin fractions, prepared by the method of Kamm and co-workers (29). The source material for preparation of the oxytocin fractions was a commercial extract provided by Kamm of Parke, Davis and Company. The countercurrent distribution between 0.05-percent acetic acid and secondary butyl alcohol proved to be highly effective. We obtained a fraction that appeared to behave like a pure compound by this criterion, and, through application of the elegant starch-column chromatographic method of Moore and Stein (30), we were able, with Pierce (31), to show that an acid hydrolyzate of oxytocin consisted of eight amino acids and ammonia.

It was now of importance to determine whether, starting from the glands themselves, material of the same potency and properties would be obtained. Therefore the oxytocin was isolated from lyophilized posterior lobes of beef pituitary glands (32). A preparation was obtained that had approximately the same distribution curve and the same potency as the preparation obtained from the concentrate. The two preparations likewise showed the same amino acid composition. The chromatogram of the amino acids in the hydrolyzed oxytocic material from beef posterior pituitary lobes is shown in Fig. 2. The amino acids were present in a molar ratio to each other of 1 to 1, and the molar ratio of ammonia to any one amino acid was 3 to 1. Molecular weight determinations indicated

a molecular weight in the neighborhood of 1000.

The sulfur content of oxytocin could be entirely accounted for by cystine. Knowing the cystine content of the purified hormone, it becomes evident, from the sulfur content of all the prewar preparations, including those of Kamm and co-workers and our preparations, that none of these preparations could have been more than 50-percent pure, regardless of the unitage ascribed to them on an arbitrary basis by reference to a standard powder. No greater purity than 50 percent could be attributed to these early preparations, even if the sulfur of the preparations were due entirely to the presence of oxytocin, which is somewhat unlikely, since sulfur-containing impurities may well have been present.

Further countercurrent distribution of the purified oxytocin involving 1000 transfers resulted in no change in composition, and this work (33) culminated in 1952 in the isolation of a crystalline flavianate of oxytocin with Pierce, the first crystalline derivative of this hormone to be isolated.

It is of interest that an oxytocic fraction was also obtained from hog posterior pituitary glands that had a distribution curve approximately the same as that from beef glands (33). In addition, the oxytocin obtained from the hog pituitary had the same amino acid composition and potency as that obtained from beef.

During the course of these studies on the oxytocic hormone, the pressor hormone, vasopressin, was also isolated from beef glands and shown to contain six of the same amino acids as oxytocin. In place of the leucine and isoleucine in oxytocin, vasopressin contained phenylalanine and arginine.

### Biological Effects

With the isolation of what appeared to be the pure hormones and the establishment of their composition, we were for the first time in a position, on a chemical basis, to be quite certain that the oxytocin was free of vasopressin, and therefore it was possible to ascertain the biological effects of oxytocin itself.

Before going into this, it might be well to mention a few of the biological activities that have been attributed to the posterior pituitary gland. I would recall to you that it was just 60 years ago that the first biological effect of the pituitary gland was discovered by Oliver and Schäfer (34). They found that extracts of the pituitary when injected into mammals raised their blood pressure—the pressor effect. Howell showed a few years later that this activity resided in the posterior lobe (35). Since that time, other biological activities of posterior

pituitary extracts were noted, particularly the uterine-contracting, or oxytocic, effect by Dale in 1906 (36); the milk-ejecting effect by Ott and Scott in 1910 (37); the blood-pressure-lowering effect in birds—the avian depressor effect—by Paton and Watson in 1912 (38); and the inhibition of urine excretion in man, the antidiuretic effect, by von den Velden in 1913 (39).

To determine the biological effects of the purified oxytocin, it was assayed for avian depressor effect against a standard powder according to the method of Coon as described in the *United States Pharmacopeia* (40) and found to possess this activity to the extent of 450 to 500 units per milligram (33). In addition to the avian depressor effect, the oxytocin was found to have the same potency, relative to the standard powder, in bringing about contractions of the isolated rat uterus—the uterine-contracting activity. The oxytocin also showed the same potency (450 to 500 units per milligram, relative to the standard powder) in bringing about

the ejection of milk. This milk-ejecting activity of oxytocin was demonstrated by tests of our purified material in sows by Whittlestone (41), in rabbits by Cross and van Dyke (42), and in recently parturient women, the latter testing having been carried out in a collaborative study with Douglas, Nickerson, and Bonsnes of the department of obstetrics and gynecology at Cornell University Medical College (43).

We thought at first that oxytocin was devoid of pressor and antidiuretic activity. However, we placed at van Dyke's disposal samples of our purified oxytocin, which he and his colleagues assayed by refined techniques. They found 7 units of pressor and 3 units of antidiuretic activity per milligram. These activities have been confirmed qualitatively and quantitatively with our synthetic oxytocin, so there is no longer any question that they are inherent properties of the oxytocin molecule (44). It might be mentioned that vasopressin, in addition to its pressor and antidiuretic effects (500 to 600

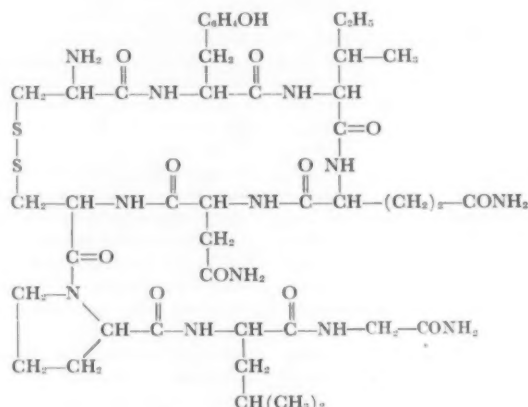


Fig. 3. Oxytocin.

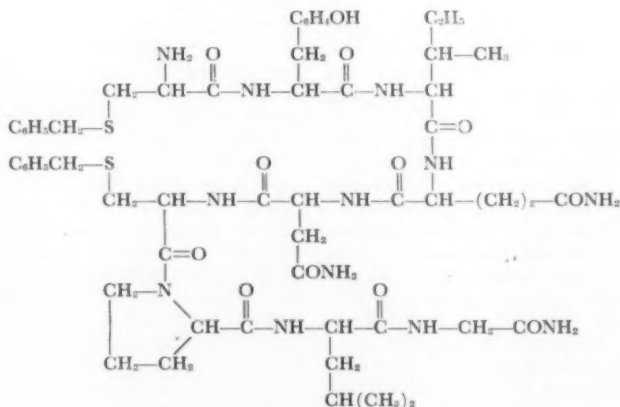


Fig. 4. Benzylated derivative of reduced oxytocin.

units per milligram, relative to the standard powder), also possesses avian depressor, uterine-contracting, and milk-ejecting activity, but the potency of vasopressin with respect to the latter three activities is only a fraction of the potency of oxytocin.

## Structure

With the purified oxytocin at hand and its composition established, we then turned to the problem of how the component amino acids were linked. Of course, there were many structures that could be written involving the eight amino acids and ammonia. The greatest difficulty in the degradative work was the scarcity of material. To obtain enough purified hormones was truly a prodigious task, as has already been mentioned. The various degradative steps were performed carried out on milligrams of material, and, in most instances, the methods had to be adapted to this scale.

Since I am attempting in this presentation to focus attention on the synthesis of oxytocin in relation to this trail of sulfur research, I shall not present the studies involving a variety of procedures in our gradual elucidation of the structure of the hormone. These researches over the course of several years with Pierce, Mueller, Turner, Davoll, Taylor, and Kunkel (45-50), and the final decisive experiments with Ressler and Trippett (51, 52) on the cleavage of performic acid-oxidized oxytocin with bromine water and on the partial hydrolysis and identification of peptide fragments, brought us to a clear-cut concept of the structure of oxytocin, a new type of cyclic polypeptide amide shown in Fig. 3 (52, 53). Although this structure was the only one that we could arrive at through the rationalization of our data, we felt that proof of this structure by synthesis of the compound was mandatory because of certain assumptions involved in postulating it.

It is of considerable interest that Tuppy, on the basis of data we had published along with some data of his own, arrived at the same structure independently (54). Tuppy's proposal was based on the data from our laboratory on composition, molecular weight, terminal groups—as worked out by our use of the Sanger dinitrophenyl end-group procedure (55)—and on the cyclic structure involving the disulfide linkage that we had established, along with his independent studies on the sequence of amino acids involving partial hydrolysis with acid and with an enzyme. The interpretation of the data and the assumptions made were quite parallel in both laboratories.

As I have already mentioned, we felt

that proof of the structure that we had arrived at had to be adduced by synthesis—that is, of course, if the synthesis were within the range of possibility. I might point out that the synthesis of this structure meant the synthesis of an octapeptide of eight different amino acids, one of them being cystine. In addition, this desired octapeptide contained three amide groupings and was a cyclic polypeptide for which no known synthetic methods were available—a cyclic pentapeptide with a tripeptide side chain. To add to the challenge was the fact that we knew the final product was relatively unstable and easily inactivated. Gentle means would therefore have to be employed.

## Background of Synthetical Approach

The clue to approaching a synthesis of this compound rested on our work with Sealock, carried out in the 1930's, on the reduction of oxytocin and the oxidation of the reduced oxytocin without appreciable inactivation at either step, which has already been discussed (20). On the basis of our postulated structure for oxytocin (Fig. 3), the reduction of oxytocin and subsequent oxidation could be interpreted as involving the opening and closing of the 20-membered ring. The reduced oxytocin would then have a linear structure containing two sulfhydryl groupings in place of the disulfide linkage in oxytocin. Furthermore, if the proposed structure for oxytocin were correct, reduction of oxytocin with sodium in liquid ammonia followed by addition of benzyl chloride should give rise to the S,S'-dibenzyl derivative of reduced oxytocin, possessing the structure shown in Fig. 4.

Since benzylation of reduced oxytocin had led to inactivation in the earlier study, the expectation was that this benzylation derivative of reduced oxytocin would be biologically inactive. With what we now knew of the structures involved, we could see no reason why treatment of the S,S'-dibenzyl derivative of reduced oxytocin with sodium in liquid ammonia should not lead to the biologically active, reduced oxytocin; oxidation of the sulfhydryl form by aeration should then lead to the regeneration of oxytocin itself, if our concepts and line of reasoning were valid.

We therefore decided to investigate benzylation and debenylation of reduced oxytocin, starting with highly purified oxytocin preparations in work with Gordon (56). Our best sample of natural oxytocin was treated with sodium in liquid ammonia followed by the addition of benzyl chloride to the liquid ammonia solution. From this reaction mixture, a product was obtained, which on analysis for amino acids had the expected com-

position, containing 2 moles of S-benzyl-cysteine along with 1 mole of each of the other seven amino acids present in oxytocin.

This material was biologically inactive. The isolated dibenzyl derivative was then dissolved in liquid ammonia, and metallic sodium was added. After the ammonia had been removed, the product was dissolved in water and oxidized by passing air through the solution at a pH close to neutral; a biologically active product was obtained. From a comparison of the physical, chemical, and biological properties of the starting and regenerated material, we were convinced that oxytocin had been regenerated from its S,S'-dibenzyl derivative. With this result, I was confident that the door was opened for a synthesis of oxytocin.

If the linear dibenzyl nonapeptide shown in Fig. 5, which possesses a carbobenzoxy group on the amino group of one of the cysteine residues, could be synthesized, it should be possible to convert this protected nonapeptide by reduction to the reduced form of oxytocin and, by subsequent oxidation, to oxytocin (see Fig. 5).

The parallelism between this approach to the synthesis of reduced oxytocin and the approach to the synthesis of glutathione, which I have already discussed, is at once apparent. In both cases, the cysteine residues present in the intermediates for the syntheses were protected by carbobenzoxy and benzyl groups, which were to be removed later in the synthesis by sodium in liquid ammonia.

## Synthesis

After a consideration of the many ways in which the synthesis of the intermediate for oxytocin might be approached, and after exploratory synthetic studies, it was decided to attempt to prepare the compound by combining the tetrapeptide amide, S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycinamide, through appropriate means, with L-isoleucyl-L-glutamyl-L-asparagine to obtain the heptapeptide amide, L-isoleucyl-L-glutamyl-L-asparaginyl-S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycinamide, and to condense the latter with N-carbobenzoxy-S-benzyl-L-cysteinyl-L-tyrosine, thus forming the desired nonapeptide amide. We concentrated on this line of approach. I should like to acknowledge the splendid collaboration of Ressler, Swan, Roberts, and Katsoyannis (53, 57) in this work.

In addition to the classical methods for the formation of peptides, other recently developed procedures were employed. We were able to utilize to particular advantage the contributions of Vaughan and Osato (58) and of Ander-

son, Blodinger, and Welcher (59). In the former case, the mixed anhydride of an N-substituted amino acid, with, for example, isovaleric acid, is used for the preparation of the peptide; in the latter method, tetraethyl pyrophosphite is the condensing agent.

In addition to using the carbobenzoxy group as a protective grouping for the amino group, we have also employed the tosyl group for this purpose. Removal of the tosyl grouping was accomplished by the use of sodium in liquid ammonia, as utilized in our work with Behrens (60) on the synthesis of  $\alpha$ -amino-N-methyl-L-histidine. The tosyl group as a protective group in peptide synthesis was first used by Schoenheimer (61), who employed a hydriodic acid-phosphonium iodide cleavage.

Concerning the specific steps in our attempted synthesis of the hormone, the tetrapeptide amide was prepared with Ressler (53, 57, 62). Ethyl carbobenzoxy-L-leucylglycinate was synthesized by the mixed-anhydride procedure of Vaughan and Osato (58). After catalytic removal of the carbobenzoxy group, according to the procedure of Bergmann and Zervas (5), the ethyl L-leucylglycinate was condensed with carbobenzoxy-L-proline, again by use of the mixed-anhydride procedure with isovaleryl chloride.

After removal of the carbobenzoxy group by reduction with hydrogen in the

presence of a palladium catalyst, the ethyl L-prolyl-L-leucylglycinate was converted to the tetrapeptide, S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycine, via the dicarbobenzoxy-L-cystinyl derivative. Ethyl dicarbobenzoxy-L-cystinyl-bis(L-prolyl-L-leucylglycinate) was saponified in aqueous dioxane at 5°C in the presence of 1 equivalent of sodium hydroxide to yield the corresponding acid. The latter was converted to S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycine according to our procedure for the removal of carbobenzoxy groups in cystine-containing compounds by the use of sodium in liquid ammonia (7) followed by benzoylation (6) of the sulfur of the reduced compound in the same medium. The crude tetrapeptide was readily converted, with the use of benzyl alcohol and dry hydrogen chloride, to the crystalline benzyl ester hydrochloride, benzyl S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycinate hydrochloride. Amination was accomplished by allowing the free base obtained from the benzyl ester hydrochloride to stand in solution in methanolic ammonia for several days at room temperature. S-Benzyl-L-cysteinyl-L-prolyl-L-leucylglycinamide was isolated from its benzyl ester hydrochloride as a crystalline hydrate.

A novel method was devised with Swan (53, 57, 63) for the synthesis of glutaminylasparagine. Harington and Moggridge (64) had already shown that

heating tosyl-L-glutamic acid under reflux with acetyl chloride gave the mixed anhydride of 1-tosylpyroglutamic acid and acetic acid, which on hydrolysis in aqueous dioxane gave 1-tosylpyroglutamic acid, and that this compound with phosphorus pentachloride gave 1-tosylpyroglutamyl chloride. They had shown that the pyrrolidone ring in these compounds could be opened with aqueous alkali but was stable to anhydrous ammonia. In our work, tosyl-L-glutamic acid was treated directly with phosphorus pentachloride. The reaction product was then coupled with L-asparagine in the presence of aqueous magnesium oxide as the condensing agent (5) to give 1-tosylpyroglutamyl-L-asparagine. The latter compound with concentrated aqueous ammonia yielded tosyl-L-glutaminyl-L-asparagine, the pyrrolidone ring having been opened by addition of the elements of ammonia. Detosylation of the tosyl dipeptide by treatment with sodium in liquid ammonia gave L-glutaminyl-L-asparagine.

For the preparation of tosyl-L-isoleucyl-L-glutaminyl-L-asparagine with Katsoyannis (53, 57, 65), tosyl-L-isoleucine was converted to the corresponding acid chloride and the latter was then coupled with L-glutaminyl-L-asparagine in the presence of magnesium oxide to give the tosyl tripeptide.

Condensation of this tripeptide with the tetrapeptide was effected by the use of tetraethyl pyrophosphite according to the general procedure of Anderson, Blodinger, and Welcher (59). Removal of the tosyl group from the protected heptapeptide amide was effected with sodium in liquid ammonia, by which the benzyl group was also removed. The resulting reduced compound was then benzylated with benzyl chloride in the same medium to yield the heptapeptide amide.

Finally, the heptapeptide amide was condensed with S-benzyl-N-carbobenzoxy-L-cysteinyl-L-tyrosine (66), a dipeptide which had originally been prepared by Harington and Pitt Rivers (67). The condensation was brought about in the presence of tetraethyl pyrophosphite to yield N-carbobenzoxy-S-benzyl-L-cysteinyl-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycinamide.

This was the compound we had set about to prepare as our proposed intermediate for the synthesis of oxytocin. If our structure for oxytocin were correct, we had every reason to believe that this compound, on reduction with sodium in liquid ammonia, followed by appropriate oxidation, would give us oxytocin (Fig. 5).

Therefore, this intermediate was treated with sodium in liquid ammonia, by which both the benzyl and carbobenzoxy groups were removed. The re-

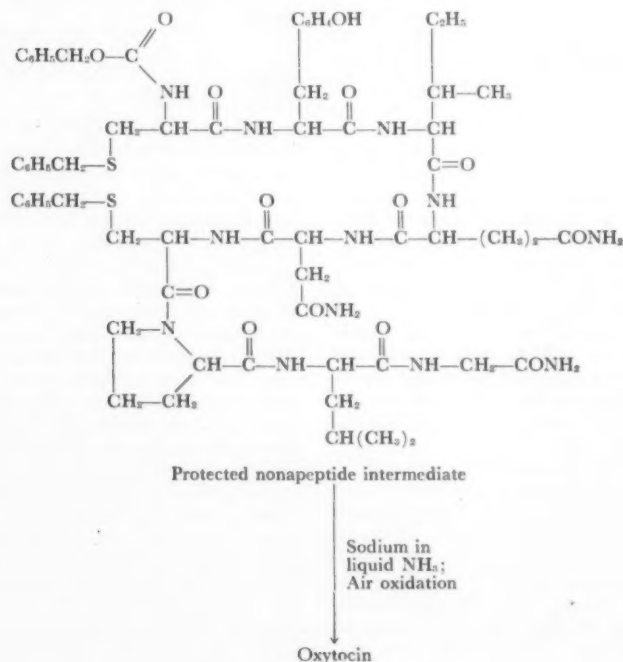


Fig. 5. Proposed intermediate leading to the synthesis of oxytocin.

duced material that was obtained after evaporation of the ammonia was oxidized by aeration in dilute aqueous solution at pH 6.5 and tested for biological activity by the rat uterine strip method (68, 69) and by the chicken vasodepressor method of Coon (70). The latter utilizes the property of oxytocin of lowering the blood pressure of the fowl and has been adopted by the *United States Pharmacopeia* as the method of assay for oxytocin (40). Based on the assumption that the synthetic material has a potency equivalent to that of the purified natural material (500 units per milligram), the yield of biologically active material, as determined by the two types of assay, ranged in several runs from 20 to 30 percent of the calculated amount from the protected nonapeptide intermediate. The yield approximated closely the yield of oxytocic activity obtainable under similar conditions from the S,S'-dibenzyl derivative of reduced natural oxytocin (56).

### Synthetic Oxytocin

The purified synthetic product, isolated by countercurrent distribution, and our best samples of natural oxytocin were assayed against each other following rigorously the procedures outlined by the *United States Pharmacopeia*. The results indicated that the activity of the synthetic material (53, 57) was indeed very close to that of the natural oxytocin (33).

This synthetic material and natural oxytocin were then compared by a battery of physical and chemical tests (53, 57). They had the same amino acid composition. They showed, within experimental error, the same optical activity, partition coefficient (in two different solvent systems), electrophoretic mobility (at two different hydrogen-ion concentrations), infrared pattern, ultraviolet spectrum, and effluent pattern from an IRC-50 resin (71).

The synthetic material formed an active flavanate that had the same crystalline form (fine, silky needles) and the same melting point as the flavanate obtained from natural oxytocin.

On treatment with bromine water, the synthetic material underwent the cleavage into two fragments encountered with natural oxytocin, both giving rise to  $\beta$ -sulfoalanyldibromotyrosine and a sulfonic acid heptapeptide (51).

Sedimentation studies on the molecular weight of natural oxytocin and the synthetic material were kindly made by Schachman and Harrington of the University of California. The natural and synthetic materials behaved identically, and the values that were obtained were in the expected range.

We were fortunate at this stage to have the collaboration of the Lying-In Hospi-

tal group of the New York Hospital-Cornell Medical Center on the use of our highly purified natural oxytocin in induction of labor and in milk ejection, for the natural and synthetic material were now compared on human subjects. The synthetic product was fully effective in stimulating labor in the human being and in milk ejection and could not be distinguished from the natural oxytocin in its action. Approximately 1 microgram of either the natural oxytocin or the synthetic material given intravenously to recently parturient women induced milk ejection in 20 to 30 seconds (43).

These comparisons of the physical, chemical, and biological properties of the synthetic product with those of the purified, natural oxytocin justified in our estimation the conclusion that the synthetic octapeptide amide is oxytocin and that the structure shown in Fig. 3 represents that of the hormone (57).

With the establishment of the structure of oxytocin, a new ring system—that is, a 20-membered ring involving a disulfide linkage—was for the first time recognized in nature. Our studies have indicated that a ring of this same size is present in vasopressin, the blood-pressure-raising and antidiuretic hormone of the posterior pituitary (72). Recently it has been shown by Sanger and coworkers (73) that a ring of the same size, involving a disulfide linkage, occurs in the insulin molecule, as part of a more involved structure.

The establishment of the structure of oxytocin and vasopressin will undoubtedly open the door to a better understanding of these hormones by the biochemist, the physiologist, the pharmacologist, and the clinician. Moreover, it should provide a suitable basis for the study of the relationship of chemical structure to biological activity in these proteinlike substances. The synthesis of oxytocin will afford a means of obtaining the compounds necessary to the study of this relationship and may, in addition, point the way to the synthesis of more complex sulfur-containing polypeptides.

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## Charles C. Adams, Ecologist

Charles Christopher Adams was a pioneer in and one of the creators of ecological perspective. Through the kindness of his daughter, Harriet Adams, I have at hand his bibliography of some 154 titles, including six unpublished works. This list makes clear not only the gradual development of his personal interests, but also his service in broadening our concepts of ecology and its role. Although it is not a matter of record, much that he accomplished was done in the face of inertia and even opposition on the part of established and conventional influences.

Adams was born in 1873. He began publishing notes on natural history before his graduation from Illinois Wesleyan University in 1895. Several papers on invertebrates appeared after he did his master's work at Harvard University in 1899, but it was his fellowship at the University of Chicago (1900-1903) that appears to have been decisive. Here his contacts with Cowles, Salisbury, and Transeau resulted in notable papers on base leveling and on Pleistocene climatic change in relation to faunal problems. Together with Transeau's paper on forest centers, these marked a resumption of serious American biogeographical study, initiated long before by Asa Gray, but with the added advantage of new information on geomorphology and Pleistocene history.

From 1903 to 1907, Adams was in museum work, first at the University of Michigan, then at the University of Cincinnati. He quickly developed the idea that the museum is a vital teaching center that is linked to the community and its natural history. This idea was to remain a guiding motive for the rest of his life;

it expressed itself at this time in his ecological survey of central and northern Michigan. In 1904 he organized and directed the Isle Royale Ecological Survey. In 1908 he returned to Illinois as associate in animal ecology, where he prepared his *Guide to the Study of Animal Ecology* and a detailed report on the various communities of invertebrates in the prairies and forests of eastern Illinois.

In 1914 he became forest zoologist of the New York State College of Forestry at Syracuse. There he organized the Roosevelt Wildlife Experiment Station and directed its activities until he became director of the New York State Museum, a position he kept until his retirement in 1943. At these two posts, much of his most significant work was done, although it was often concealed behind the routine into which it was incorporated. He continued his idea of ecological surveys at the Palisades, Mount Marcy, Alleghany State Park, and in the Rochester region. He wrote much on wildlife and fisheries in relation to forestry, and after an initial paper on conservation in 1915, he gave that problem increasing emphasis.

Ecologists, notably in the Forest Service, had long appreciated the possibilities of their subject as an applied science. But it seems to me that Adams did more than any other individual in America to give this idea comprehensive form. In 1930 he turned his attention to the synthesis with human ecology, using the Shaker collection in the Albany Museum as a basis. In orderly fashion, he proceeded to enlarge the scope of his interest, through schools, water resources planning, and regional and urban planning.

He brought to the attention of ecologists the work of Mumford, Mackaye, Lindeman, Benedict, and Patrick Geddes, whose concepts of the living museum and of ecological planning and whose experience, in some respects, paralleled his own. Adams organized symposia on human ecology and insisted that ecology, with its tremendous possibilities for human good, ought to be underwritten on the same scale as geography, geology, and the physical sciences.

Keenly aware that ecology is a study of process, he saw the importance to it of records and archives, and of some central institute where these could be conserved and where workers could be housed with facilities fitting their value to society. He never ceased trying to rouse ecologists to appreciate their own importance, warning them that unless they could do so, their job would be taken over eventually by others.

One of the founders and a past president of the Ecological Society of America, he was also active in the Association of American Geographers. He maintained an extensive and lively correspondence, and he was unusually enterprising in hunting up those whose ideas interested him. Physically he was stout and vigorous. His tastes were simple, but his energy prodigious. His home was itself a museum and library combined, overflowing with books and pamphlets which he governed by his own mysterious kind of order.

At the time of his death in 1955, he was working on a *Guide to the Study of Human Ecology: The Dynamics and Processes of Orientation and Integration*. Like his earlier guide to animal ecology, this was to be an annotated bibliography, but so set up as to be immensely useful to any serious student.

His library, notes, and other material have been presented by his daughter to Western Michigan State College at Kalamazoo, where they will be kept available, as he wished that all important ecological materials might be, for future workers. There they will form a nucleus for the Charles C. Adams Center for Ecological Studies under the direction of Daniel Jackson.

PAUL B. SEARS

*Yale University  
New Haven, Connecticut*

## E. R. Dunn, Herpetologist

Emmett Reid Dunn had an extraordinary grasp of herpetology on a world-wide basis. His phenomenal memory and his knowledge of animals, their classification, their distribution, and the literature written about them were such that he was the oracle to whom colleagues and students turned repeatedly for information and guidance. As a college professor, an excellent field and museum man, and as an eminent authority, he was in a position to make large and important contributions to zoology. This he did in more than 200 published works.

Dr. Dunn, who was known as "Dixie" to his close friends, was born in Alexandria, Virginia, 21 November 1894. His first introduction to herpetology came, naturally enough, when his boyhood activities placed him in possession of sundry frogs, snakes, and turtles. But unlike most lads, who keep such pets as a passing fancy, young Emmett took them seriously and was soon visiting the National Zoo and Museum in search of knowledge about them. His schooling took him to Haverford College and later to Harvard where he received his Ph.D. in 1921. While teaching at Smith College he met and married a fellow teacher, Alta Merle Taylor, who became his constant companion in the field and assisted in the preparation of many of his papers. A few years after joining the faculty of Haverford College in 1929 he became David Scull professor of zoology, a chair that he occupied until the time of his death, 13 February 1956. He had been ill for a year.

Geographically, Dr. Dunn's special interests at first embraced the United States, but they soon encompassed a large segment of the Neotropical region. Early expeditions took him into the mountains of his native Virginia and into the fastnesses of the southern Blue Ridge Mountains. There he became acquainted with the extraordinarily rich salamander fauna of the region, and his early collecting activities and his lively curiosity

about the group culminated eventually in the publication of his *Salamanders of the Family Plethodontidae*. In the preface to this classic addition to herpetological literature, he gave credit to the late Leonhard Stejneger, of the United States National Museum, for focusing his attention upon salamanders instead of snakes, a more glamorous group that even to this day appeals most to young herpetologists. Despite this advice, Dr. Dunn did not neglect the serpents, for he published many papers about them, and a number of snakes were included among the several dozen new species of reptiles and amphibians that he discovered and made known to science.

It was in the American tropics, however, that Dr. Dunn did the bulk of his field work. He collected in Cuba and Jamaica, he spent a year in Colombia, he traveled extensively in Mexico, and his expeditions to Panama and Costa Rica exceeded a dozen in number. In town or in the wilderness he was constantly collecting specimens, seeking novelties and adding to his great fund of knowledge of the Neotropical fauna. One of his most rugged and most ambitious explorations took him into the little known Peninsula de Azuero, that thrusts southward west of the Gulf of Panama like the heel of a misshapen shoe. On these trips he was aided by a grant from the American Philosophical Society, by a Guggenheim fellowship, and by assistance from the Gorgas Memorial Institute of Tropical and Preventive Medicine. In collaboration with Dr. Herbert C. Clark, director of the Gorgas laboratory, Dr. Dunn undertook a unique census of the snakes of Panama. In clearing land for banana plantations, the laborers frequently encountered serpents that they promptly decapitated with their machetes. Through the cooperation of the overseers, the heads were dropped into containers of preservative, and they eventually reached Dr. Dunn's office. Several thousand heads, plus a considerable

number of small snakes that were preserved entire, furnished a rich source of data for snake-population studies and an analysis of the snake fauna in the vicinities of several collecting stations in Panama.

Only twice did he venture into the Old World. He was a member of the Douglas Burden Expedition to Komodo in the East Indies in 1926, and he used part of his Guggenheim fellowship to examine types of snakes in European museums in 1928.

Dr. Dunn served at one time or another on the staffs of the Academy of Natural Sciences of Philadelphia, the American Museum of Natural History, the Museum of Comparative Zoology, and the United States National Museum. One of his major, but virtually unknown, contributions to herpetology was his work in curating the reptile and amphibian collection at the Philadelphia Academy, for which he received no compensation. This important collection, rich in types and historic significance, had long been inactive, largely because the academy staff did not include a herpetologist. For almost a decade, Dr. Dunn devoted at least one full day each week to the formidable chore of rearranging and labeling the collection, preparing a card index, and identifying and cataloging a large number of specimens that had accumulated over a period of years. In this work he was assisted by Mrs. Dunn and, during certain periods, by his graduate students.

Although he was a specialist, and an accomplished one, Dr. Dunn never lost his perspective. In his teaching, his lectures, and his conversations with colleagues, it was obvious that his thinking was based on a comprehension of natural history on a global basis. He was fluent in discussions that concerned geology, physiography, animal distribution, evolution, comparative anatomy, and many other subjects. His papers on such general topics as the classification and phylogeny of the salamanders, the criteria for vertebrate subspecies, species, and genera, and the key and arrangement of the New World genera of the snake family Colubridae give some indication of the breadth of his interests.

An appreciation of Dr. Dunn's knowledge and ability has been expressed by a colleague—"What a shame that a man who knew so much and who could have contributed so much more to his field should have died so young."

ROGER CONANT

Philadelphia Zoological Garden  
Philadelphia, Pennsylvania

*A great nation assailed by war has not only its frontiers to protect, it must also protect its good sense.—ROMAIN ROLLAND.*

## News of Science

### Meteorology and Atomic Energy

The executive committee of the World Meteorological Organization has announced the establishment of a 4-member panel of specialists to study the meteorological aspects of the peaceful uses of atomic energy, with particular emphasis on the movement of radioactive waste products in the atmosphere. The following scientists were named to the panel: A. A. Danilin, U.S.S.R.; B. Guilmet, France; P. J. Meade, United Kingdom; and A. I. Wexler, United States.

The panel's terms of reference mention the need to insure that techniques arising from this field of activity be used to assist the science of meteorology in every possible way. Among such techniques is the use of radioactive tracers in the study of large-scale movements of air masses or ocean currents.

The executive committee has also announced its decision that there is no reason to conclude that the nuclear explosions which have taken place have had any large-scale effect on the weather. The committee therefore agreed to discontinue its inquiry into this question but to keep the matter under review in the light of any information that might be forthcoming in the future.

### Junior Academies of Science

With a serious scientific manpower shortage facing our country it is obvious that the young scientist must play a very important part in the world of tomorrow. The junior academy of science movement is one of the active interests of the AAAS Science Teaching Improvement Program in its work of discovering and developing scientific talent in American youth.

Twenty-five states and three cities report having a junior academy of science. The academies may have science-club memberships, individual memberships, or be organized along either of these patterns. Although the junior academies are primarily an activity at the high-school level, 18 of them include junior-high students and one has only junior-college students.

The junior academies are often financially supported by means of dues, registration fees, sponsoring senior academies, bequests, memorials, grants, or other sources. The academies are usually directed by an advisory committee that is under the control of the senior academy. Students occupy the major offices in 18 of the organizations.

All but two of the academies have at least one meeting a year with the senior academy. The contact with the senior scientists of the state is usually the most inspiring part of the program, and the senior scientists are always impressed by the talent observed among the juniors.

The presentations of student research are the most important part of the junior academy meetings. The research may be presented as an exhibit, a demonstration, or a paper. The projects are not always technically accurate and students do not have the scientists' knowledge that would lead them to limit their fields of endeavor. Consequently, some highly technical scientists have expressed their doubt as to the value of projects, but one needs only to talk to junior members at their meetings to recognize the value of such projects in the stimulation of scientific thinking at the high-school level.

Lectures are frequently given at the junior academy meetings by distinguished state or national scientists who are leaders in their fields. Most of the junior academy programs include trips to museums, industrial plants, and other places of scientific interest.

The stimuli of attending meetings, sharing ideas on projects, and meeting senior scientists make attendance at junior academy meetings a coveted trip for students, but in many states further awards are given to participants. These awards may be cash, certificates, scholarships, loving cups, ribbons, plaques, or subscriptions to science magazines. Two honorary annual memberships in the AAAS are available to each academy. In four states outstanding teacher-sponsors are also rewarded by citations, pens, keys, or summer scholarships that may be used for graduate work.

Several of the junior academies publish announcements, information, scientific articles, book reviews, or similar features. The junior academies that have

such publications usually maintain a higher level of interest than the others. A few junior academies maintain speaker and counselor committees by means of which college and industrial personnel are made available as speakers and advisers for science clubs, classes, or other meetings.

In some states weekly radio and television programs are prepared. In others Kodachrome slides of projects are available for loan. Coprojects of many kinds with senior scientists have proved attractive to many students.

Junior academies often cooperate with state science education sections to aid in bringing new fields of science to the attention of high-school teachers. A recent education survey points to the secondary-school science teachers as those most responsible for the early identification and channeling of potential scientists. The junior academies of science are designed to assist the secondary-school teacher in appealing to superior students and guiding them along the pathway of science. There is a definite place for these junior science activities in helping to alleviate the manpower shortage.

THELMA HEATWOLE

Woodrow Wilson Educational Center,  
Staunton, Virginia

### Socio-Psychological Prize Judges

Judges for the 1956 AAAS Socio-Psychological prize essay contest are Fred L. Strodbeck, University of Chicago Law School; Raymond V. Bowers, chief of the social science plans division, Air Force Personnel and Training Research Center, Lackland Air Force Base; and Kimball Young, department of sociology, Northwestern University. Announcement of the contest and the conditions of competition appeared in the 30 Mar. issue of *Science*. The deadline for receipt of entries is 1 Sept.

### Civil Service Science Salaries

Philip Young, chairman of the U.S. Civil Service Commission, made several comments about salaries for scientists and engineers during a recent address before the Society of Personnel Administration. Young said he was convinced "some adjustments in pay" were warranted for scientific positions. He also indicated that the Administration might ask Congress to give it the authority to pay expenses for pre-employment interviews of applicants for hard-to-fill jobs, as well as travel and moving expenses of new appointees to their first posts of duty.

He observed that the salaries paid scientists and engineers working on govern-

ment contracts were "substantially higher" than those paid by the Government. He suggested that Federal agencies, in awarding contracts for scientific research work, "consider the impact of the salaries paid by their contractors on salaries in the whole field."

### AEC Headquarters

The U.S. Atomic Energy Commission has awarded to John McShain, Inc., of Philadelphia a contract in the amount of \$8,828,000 for construction of the commission's new headquarters building near Germantown, Md. The McShain bid was the lowest of the 13 received. The contractor is expected to begin work at once on the 109-acre site, which is 23 air miles from Washington.

The 4-story, wing-type structure of monolithic reinforced concrete faced with brick is scheduled for completion in late 1957. It will house about 1600 people, including commission employees, military personnel, and others assigned to work at AEC headquarters.

In addition to the main building, there will be a cafeteria designed to accommodate 450 people and a 300-seat auditorium. Auxiliary buildings include a warehouse, garage, boiler house, and cooling tower. Cost of the entire project, including all buildings, land, landscaping, and utilities and other expenses is estimated at \$10 million. The architect for the project is Voorhees, Walker, Smith, and Smith of New York.

### New Canadian Clinics

Canada's first clinic for sex deviates was opened in May by the Ontario Department of Health. Called the Forensic Clinic, it is to function as an adjunct of the University of Toronto in 14 rooms that have been especially set aside.

A modern examination and treatment center is planned, and although initially the director will have only two full-time assistants, the staff is expected to expand rapidly as the courts and the public become more familiar with the services available.

The clinic is the first of a series that is to be established in university cities across the province. The second will probably be in London, where it would operate in cooperation with the University of Western Ontario.

### Heart Disease Mortality in Women

Heart attacks now kill as many women as men, according to Stanley W. Hartroft, chairman of the department of pathology at Washington University (St.

Louis). He presented some results of recently completed statistical studies at the annual meeting of the American Chemical Society's New York Section.

Data assembled on 8000 autopsies showed that between 1910 and 1940 twice as many men as women died from myocardial infarction, whereas from 1940 to 1955 approximately as many women as men succumbed. The narrowing of the gap between the sexes was attributed to the finding that, in the age group over 60 years old, more women than men had become victims of heart disease. Hartroft commented:

"I almost hesitate to suggest it, but perhaps these women over 60 who are now dying more frequently of myocardial infarction than are the men, represent a group of our population that started smoking for the first time twenty years ago."

Wilbur Thomas and Kyu Lee, also of Washington University, collaborated in the study.

### Pygmies in New Guinea

The Rev. Martin Gusinde, professor of anthropology at Catholic University of America, has left on a 4-month expedition to New Guinea, where he will study a group of pygmies who live in a remote region which has never been visited by a white man. The American Philosophical Society is sponsoring the trip.

The Australian government has extended a special invitation to Gusinde to enter the interior of the unmapped and unexplored territory, which is 12,000 feet above sea level in the Schrader Mountains south of the Ramu River in the Northeast section of New Guinea. To reach his destination, Gusinde anticipates a 4- or 5-day walking trip up the mountains accompanied by a few native Papuans, a friendly people living near the sea. He will have to travel through areas inhabited by bands of head-hunters.

### News Briefs

■ Some Soviet scientists hold a hope that someday there will be a transcontinental railroad across the Bering Strait to link the United States and the U.S.S.R. They also envision a dam project that might create artificial warm currents in the Bering Sea and perhaps change the climatic conditions in the northern regions of both countries.

These ideas were discussed recently before a civic group in Hyattsville, Md., by Aleksandr I. Zinchuk, first secretary of the Soviet Embassy. He also commented that his nation has been speculating about a project to divert Siberian

rivers into arid Central Asia instead of permitting them to empty into the Arctic Ocean.

■ The Central Laboratories for Scientific and Industrial Research of Hyderabad State, India, have been taken over by the Council of Scientific and Industrial Research, Government of India. Under the new name of Regional Research Laboratory, Hyderabad, the facility becomes the council's first regional laboratory.

S. Husain Zaheer remains as director, and the research staff continues as before. However, the change assures the fulfillment of plans that were originally made for the laboratory 4 years ago. These plans could not be executed because of the state's financial difficulties.

■ The Associated Press reports that Bruno Pontecorvo, the Italian-born atomic scientist who joined the U.S.S.R., appeared on 16 May in Moscow at a conference on the physics of high-energy particles. Twelve American nuclear physicists, including Emilio Segrè, with whom Pontecorvo once collaborated, attended the conference. This is the first time that Pontecorvo has been seen by non-Communist Westerners since he held a news conference in Moscow 14 months ago. More than 400 Soviet physicists, and some 60 others from Britain, France and other countries, participated in the meeting.

### Scientists in the News

BART J. BOK, codirector of the radio astronomy project at the George R. Agassiz Station of Harvard University, and a member of the university's staff for 27 years, has accepted an appointment to direct the Commonwealth Observatory of Australia, effective 1 Feb. 1957. He will be professor of astronomy in the Research School of Physical Sciences, Australian National University, Canberra. Control of the observatory is expected to be transferred to the university shortly. Bok succeeds R. v. d. R. WOOLLEY, who has gone to Great Britain as Astronomer Royal in charge of the Royal Greenwich Observatory at Herstmonceux.

The Commonwealth Observatory is a principal center for the observation of the most intricate part of the Milky Way, which can be studied only in the Southern Hemisphere. The new 74-inch reflector telescope is one of the two largest such instruments in the Southern Hemisphere. Associated with the observatory are the Yale-Columbia Station, and a station of the Uppsala Observatory of Sweden.

Bok has had a life-long interest in

Milky Way research, and in recent years he has also become a leader in radio astronomy. In Canberra he will concentrate primarily on optical research on the Southern Milky Way, but will work in close collaboration with the radio astronomers of the Radio-Physics Laboratory at Sidney.

PEYTON F. ROUS, member of the Rockefeller Institute, received the Kovalenko medal of the National Academy of Sciences during its recent annual meeting. He was honored for his contributions to experimental medicine.

Very early in his career Rous observed an association between viruses and tumor growth. Because his observation came at a time when knowledge of viruses was meager and cancer research was in its infancy, the significance of this relationship was not recognized. Today the viral etiology of tumors is a major area of cancer research, and for the past 20 years Rous has been at the forefront of this activity. Rous has also conducted significant research in the physiology and pathology of the liver and the physiology of the blood vessels.

ROBERT H. LYDDAN has been named assistant director of the U.S. Geological Survey. Since July 1955 he has been regional engineer at the Atlantic regional office, topographic division, Arlington, Va.

HOWARD S. COLEMAN, who formerly directed the Scientific Bureau of the Bausch and Lomb Optical Company, has been appointed manager of the company's research and engineering division.

FARRINGTON DANIELS, chairman of the department of chemistry at the University of Wisconsin, recently presented the 1956 Remsen memorial lecture of the American Chemical Society's Maryland Section. He spoke at Johns Hopkins University on "Solar energy utilization."

The Remsen lectures were established in 1946 in memory of Ira Remsen, first professor of chemistry at Johns Hopkins and second president of the university. He was president of the ACS in 1902.

CHARLES N. FREY, lecturer and consultant at Massachusetts Institute of Technology, will receive the 1956 honor scroll of the New York Chapter of the American Institute of Chemists in recognition of his professional accomplishments throughout his career. Frey, for many years director of research and development of Fleischmann Laboratories, Standard Brands, Inc., will receive the award during the chapter's meeting on 7 June at the Commodore Hotel, New York.

JOHN D. BECK, professor of veterinary medicine at the University of Pennsylvania, has been named chief of staff for the new Margaret M. Caspary Center for Veterinary Research, which is to be built at 10-12 Bond St., New York. This is opposite the Ellin Prince Speyer Hospital, 350 Lafayette St., where he will also be chief of staff. Both organizations are administered by the New York Women's League for Animals. Beck is expected to continue his affiliation with the university's faculty on an associate basis.

DAVID L. COFFIN, pathologist for the Angell Memorial Hospital in Boston, Mass., and research associate and instructor in pathology at Harvard Medical School, has been named director of research by the League. GEOFFREY W. RAKE, research professor of microbiology in medicine in both the School of Medicine and the School of Veterinary Medicine at the University of Pennsylvania, will act as chairman of the research committee and of the League's board of scientific advisers.

The League has announced the receipt of a grant of \$3 million from the estate of the late Alfred H. Caspary, to be used for the establishment of the Caspary Center. Construction of the ten-story building will begin in the fall. Development of the center's research program will give increased emphasis to the affiliation, which was set up in September 1954, between the University of Pennsylvania School of Veterinary Medicine and the New York Women's League for Animals. At that time an institute for veterinary research was established by the League and two laboratories were provided in the Speyer Hospital.

An agreement has been reached with the University of Pennsylvania for the exchange of personnel and information that is expected to be beneficial to both institutions. Studies of the diseases of small animals will be emphasized in the new research center. The laboratories will be staffed and equipped to conduct both basic and clinical research.

FRANK R. CALDWELL, an experimental physicist who has been associated with the National Bureau of Standards since 1920, has been named head of the combustion controls section in the bureau's mechanics division. Caldwell helped develop the first practical jet exhaust afterburner and has led a long-term project on combustion research since 1948.

WILLIAM A. McCLELLAN, Oxford, Ohio, general practitioner, has been appointed assistant director of the department of general practice at the University of Tennessee College of Medicine in Memphis.

WEIKKO A. HEISKANEN, director of the Institute of Geodesy, Photogrammetry and Cartography at Ohio State University, has received the William Bowie medal of the American Geophysical Union.

J. G. MACHUTCHIN, formerly chemical production manager of the commercial products division, Atomic Energy of Canada, Ltd., has been appointed director of research for radioactive materials at the Bloomsburg, Pa., laboratories of the United States Radium Corporation.

Assisting in U.S. Radium's accelerated research program will be D. L. PROSER, formerly assistant chief inspector of laboratories at Canadian Arsenals, Ltd., Nitro, Quebec, who has joined the laboratories as research chemist.

IAN R. MACGREGOR, associate professor of chemistry at the University of Cincinnati, will relinquish teaching duties next September to become an assistant dean of university administration.

Z. V. HARVALIK, professor of physics at the University of Arkansas, has received a year's leave of absence, effective in August, to accept an assignment with the U.S. Army Corps of Engineers at Fort Belvoir, Va., where he will establish a basic research laboratory in the Engineering and Research Development Laboratories.

SAMUEL MARTIN, associate professor of medicine and assistant professor of bacteriology at the Duke University School of Medicine, has been appointed head of the department of medicine at the University of Florida College of Medicine; he is also coordinator of the J. Hillis Miller Health Center Study.

Eight teachers have received awards from the American Academy of Arts and Sciences for outstanding teaching in science and mathematics in New England secondary schools. The awards were made from the academy's Elizabeth Thompson Science Fund. The recipients were MALCOLM D. CAMPBELL, Dorchester High School, Boston, Mass.; DOROTHY W. GIFFORD, Lincoln School, Providence, R.I.; LORNE F. LEA, St. Paul's School, Concord, N.H.; CLIFFORD NELSON, Weeks Junior High School, Newton Centre, Mass.; JOSEPH H. ROHLOFF, Aldrich High School, Warwick, R.I.; MARCO SCHEER, Nashua High School, Nashua, N.H.; SISTER MARY WALTER, Our Lady of Perpetual Help School, Roxbury, Mass.; and CLAIBORNE H. YOUNG, Plymouth High School, Plymouth, Mass.

STANLEY H. LANGER of the U.S. Bureau of Mines, Synthetic Fuel Research Branch, Pittsburgh, Pa., has been selected by the American Chemical Society's division of gas and fuel chemistry to receive the first bituminous coal research award for his paper on "The chemistry and structure of coal: I, Optical activity in oils derived from coal."

EVA SHIPSTONE, chairman of the psychology department of Isabella Thorburn College in Lucknow, India, will study social relations next year at Radcliffe College.

MAX E. BRETSCHGER, president of the Becco Chemical Division, Food Machinery and Chemical Corporation, announced his retirement on his 30th anniversary with the company. He will continue to act as senior technical adviser. FREDERICK A. GILBERT succeeds Bretschger as president of the division.

ROBERT B. DUFFIELD, associate professor of chemistry and physics at the University of Illinois, will head the chemistry program of the General Atomic Division laboratory of the General Dynamics Corporation in San Diego, Calif.

LYOYD P. SMITH, chairman of the department of physics at Cornell University, will join the Avco Manufacturing Corporation on 1 July as president of the Research and Advanced Development Division and vice president of the parent company. In announcing the appointment, Avco revealed that it plans substantial further expansion of the division, which now has installations at Stratford, Conn., and Everett, Mass.

ALBERT H. STEVENSON has been appointed chief sanitary engineer of the Division of Indian Health by the U.S. Public Health Service. He succeeds HUGH R. McCALL, who has retired. Previously Stevenson served as chief sanitary engineer in the national office of the Federal Civil Defense Administration in Battle Creek, Mich.

JOHN C. BUGHER, director of medical education and public health for the Rockefeller Foundation, New York, has received the 1956 Howard Taylor Ricketts award of the University of Chicago.

HERMAN BEERMAN, chairman of the department of dermatology at the University of Pennsylvania, will be the guest moderator of the Clinico-Pathologic conference of the Pacific Dermatologic Association that is to take place in Honolulu, Hawaii, 24-28 June 1956. He will also give a paper on "Dermatopathology in research" as guest speaker.

MARION E. KENWORTHY, professor of psychiatry at Columbia University and pioneer educator in psychiatry, social work, and mental health, has announced her retirement. The recent Founder's Day celebration at the New York School of Social Work, Columbia University, was dedicated to Dr. Kenworthy, who has been associated with the school for 36 years. Approximately 1000 psychiatrists, social-work educators, practitioners, and friends attended the program, which included an announcement that friends and admirers of Dr. Kenworthy had contributed \$308,000 of the \$400,000 that is necessary for the endowment of a Marion E. Kenworthy professional chair in psychiatry at the school. This amount was given or pledged in the first 3 weeks of an informal drive.

William C. Menninger of the Menninger Foundation, Topeka, Kan., who was principal speaker, paid tribute to Dr. Kenworthy for her contributions to the "enrichment of training in social work." An exhibit at the school included a letter from President Eisenhower.

A graduate of Tufts Medical School, Dr. Kenworthy began in 1921 to teach regular psychiatric courses—she gave a lecture series the previous year—and also to practice psychoanalysis. In her work she has helped advance the study of child behavior, delinquency and emotional disturbance, and the training of social workers.

### Recent Deaths

WALTER S. ADAMS, Pasadena, Calif.; 79; former director of the Mount Wilson Observatory; 11 May.

JOHN CATON, Phillipsburg, N.J.; 76; founder of the Chrysler Institute of Engineering; former professor of automobile engineering and dean of the engineering school at the University of Detroit; 16 May.

MELVIN L. ENGER, Escondido, Calif.; 75; dean emeritus of the University of Illinois College of Engineering; 13 May.

JOSEPH S. FRIEDMAN, Johnson City, N.J.; 57; senior research chemist of the Ansco Corporation and a specialist in color photography; 10 May.

EDWARD M. GILBERT, San Marcos, Tex.; 80; professor emeritus of botany at the University of Wisconsin; 23 Apr.

THOMAS A. GONZALES, New York, N.Y.; 78; retired chief medical examiner for New York City; professor emeritus of forensic medicine at the New York University-Bellevue Medical College and coauthor of *Legal Medicine and Toxicology*; 14 May.

ARTHUR V. HOLLENBERG, Mor-

ris Plains, N.J.; 45; research physicist with the Bell Telephone Laboratories; 12 May.

AUSTIN R. MIDDLETON, Louisville, Ky.; 76; professor of biology and founder of the department of biology at the University of Louisville; secretary of AAAS Academy Conference 1949-50 and its president in 1952; 11 Apr.

WILLIAM COOK SPAIN, New York, N.Y.; 64; authority on allergy; professor of clinical medicine at the New York Post-Graduate Medical School of New York University; 12 May.

### Education

■ A gift of approximately \$500,000 has been made to Tulane University by Mr. and Mrs. Percival Stern of New Orleans through the Percival Stern Foundation for the establishment of a nuclear physics laboratory that is to be named the Percival Stern Laboratory of Nuclear Physics. Terms of the gift provide \$100,000 for setting up the laboratory and not less than \$15,000 a year for a period of 25 years for its maintenance.

■ The Seton Hall College of Medicine and Dentistry, Jersey City, N.J., will admit its first class in September. A 16-story building that is part of the Jersey City Medical Center is being remodeled for the preclinical departments and administrative offices. The Medical Center will be the chief clinical teaching facility of the college. This center is the largest in the state and is one of the most complete and modern hospital units in the country. It has a capacity of about 1700 beds.

The dean of the College of Medicine is Charles L. Brown, former dean and head of the department of medicine at Hahnemann Medical College and Hospital. Merritte M. Maxwell, who is dean of the College of Dentistry, has had 35 years of service in the U.S. Navy, most of it in the Dental Corps, where he has been director of a number of dental activities and in charge of internship and residency programs.

Other members of the faculty are as follows.

*Department of anatomy:* professor and head of the department, effective 1 June, Pinckney J. Harman, former associate professor at the New York University-Bellevue Medical Center; professor, effective 1 June, Charles M. Berry, former associate professor at Cornell University Medical College. The department has four assistant professors and one instructor.

*Department of physiology:* professor and head of the department, effective 1 Feb. 1956, David F. Opdyke, former head of the department of physiology at

the Merck Institute for Therapeutic Research. The department has two assistant professors.

*Department of biochemistry:* professor and head of the department, effective 1 July, Raymond L. Garner, associate professor of biological chemistry at the University of Michigan School of Medicine.

*Department of dental anatomy:* ad interim appointment as chairman of the department, effective 1 July, Robert L. Lang, associate professor at the University of Oregon College of Dentistry.

■ A radio astronomy observatory is being established near Grafton, N.Y., by Rensselaer Polytechnic Institute on the 820-acre wooded tract that was left to the institute by the late John A. Sampson. The first installation, antenna and instruments for measuring the degree to which radio waves from outer space are absorbed in the ionosphere, will be open by early fall.

Another 6 months will probably be required to put into operation the second project, an interferometer for locating the places on the surface of the sun from which outbursts of radio noise erupt and for determining the subsequent movements of the outbursts.

Funds for initial development are a \$5000 grant from the R.P.I. board of trustees, and a \$10,000 grant from the Research Corporation, New York. In addition, the U.S. National Committee for the International Geophysical Year has invited the new radio observatory to be a participant in the IGY and has made \$2000 available toward the expense of that participation.

■ More than 60 secondary-school science teachers, under the joint sponsorship of the National Science Teachers Association and the Connecticut Science Teachers Association, recently attended a 1-day institute that was presented by the staff of the New England Institute for Medical Research. The purpose of the special meeting was to inform the teachers about new developments in biology, chemistry, and physics and to demonstrate through a wide variety of experiments how the teachers could illustrate such trends easily and economically in their own classrooms.

■ The Southwestern Research Station of the American Museum of Natural History reports that at the end of its first year of operation 47 investigators representing 14 different institutions in 12 states have taken advantage of its facilities. The station was opened by the museum in the spring of 1955 as a permanent, year-round laboratory for research on the diverse fauna, flora, geology, and paleontology of the desert and semi-arid

areas in the Southwest and in northern Mexico.

The station, which was established through the interest and support of David Rockefeller and then aided by the contributions of others, is located near Portal, Ariz., on the eastern slope of the Chiricahua Mountains, within the limits of the Coronado National Forest. A scientist making a trip from the base of the mountains to their crest would have to cross two different types of desert, a grassland, and a woodland before reaching the evergreen forests at the summit, thereby covering five different "life zones." The station is probably the only research laboratory that can provide such variety.

The research workers who studied there in 1955 represented nine fields of scientific inquiry: arachnology, entomology, mammalogy, ornithology, botany, parasitology, herpetology, paleontology, and general natural history. The station's quota of visitors for the coming summer has been filled for some time, but applications are still being accepted for the fall and winter.

■ Next fall Hofstra College will offer a bachelor of arts degree in geology. The college already offers the degree of bachelor of arts in biology and geology, and bachelor of arts in chemistry and geology.

### In the Laboratories

■ More than 1475 employees of the Radio Corporation of America are taking courses at colleges and universities outside working hours under the corporation's tuition loan and refund plan. Under the plan, employees may borrow the money to pay the tuition for college courses. The amount is refunded after the successful completion of the work. Employees who choose to pay for courses themselves also receive refunds when the work is completed. During 1955 R.C.A. spent \$168,900 in education reimbursements.

■ A particle bank has been established by the Stanford Research Institute, Menlo Park, Calif., to aid academic, industrial, and governmental laboratories that require powders with known characteristics for their research activities. The preparation and standardization of such materials by individual scientists or laboratories often involve the expenditure of a substantial amount of time and money. After work with these standardized materials is completed, they are usually shelved or discarded.

The new particle bank will act as a depository and distribution center for these materials. Samples will be made

available to interested organizations for a nominal handling charge. Information regarding donations and requests for information about the availability of powders with specified characteristics should be addressed to the Particle Bank, Stanford Research Institute, Menlo Park, Calif.

■ Stockholders of Baird Associates, Inc., and the Atomic Instrument Company, both of Cambridge, Mass., have approved a merger of the two organizations that is to take effect on 1 June. The new company will be known as Baird Associates-Atomic Instrument Company. Baird manufactures optical-electronic equipment and Atomic Instrument makes instruments and components for the electronic and nuclear fields.

■ The Atomic Energy Commission has announced an expanded program for the procurement of high-purity zirconium metal and hafnium oxide to meet the increasing reactor development requirements. To assure a future supply of the materials, 5-year contracts have been signed with three new commercial suppliers who were among 10 firms that submitted proposals: National Distillers Products Corporation, which will supply 1 million pounds annually from new facilities to be constructed at Ashtabula, Ohio; NRC Metals Corporation, a subsidiary of the National Research Corporation of Cambridge, Mass., which will supply 700,000 pounds annually from a plant to be constructed near Pensacola, Fla.; and Carborundum Metals Company, which will supply 500,000 pounds annually from a new plant to be constructed at Parkersburg, W.Va. The contracts call for the annual delivery of 2.2 million pounds of zirconium, subject to the availability of funds, at an average cost of about \$14 million a year.

■ The U.S. Atomic Energy Commission has selected the proposal of the Babcock and Wilcox Company to design, fabricate, and operate a liquid metal-fueled reactor experiment. This reactor is the seventh type chosen by the commission for its research program to develop economical electric power from nuclear fuels. Other types are pressurized-water, homogeneous, fast-breeder, boiling-water, sodium-graphite, and organic-moderated. In addition, studies are under way on the gas-cooled reactor concept.

■ Beckman Instruments, Inc., has established a new data and control systems department in its plant at Fullerton, Calif. The department is managed by Taylor C. Fletcher, previously manager of Beckman's industrial instruments group.

## Reports and Letters

### New Color Test for Thiols and Thioesters

In the course of experiments with homocysteine peptides (1), it was discovered that, when the products of the reaction between N-ethyl maleimide (NEM) and thiols are made alkaline, a red color develops (2). Under the proper conditions, this reaction is extremely sensitive. The color is much more stable than that given with nitroprusside, and, in contrast to the iodine-azide reaction, it is not given by disulfides or thioethers.

This reaction, the mechanism of which is still obscure, shows a number of interesting peculiarities: (i) The color is unstable in the presence of water, probably owing to hydrolysis of the imide ring. It is much more stable in ethanol and isopropanol but not in methanol. (ii) The color is an acid-base indicator, since it is discharged by acid and reappears upon the addition of alkali. (iii) The maximum color is not produced with equimolar concentrations of thiol and NEM. It is greatly potentiated by an excess of NEM. Thus  $10^{-5}M$  concentrations of sulfhydryl can easily be detected but only if the NEM concentration is of the order of  $0.1M$ . (iv) The color is not produced when the NEM is exposed to alkali prior to the addition of thiol. This is undoubtedly due to the instability of NEM in alkaline solution (3).

It is interesting to note that Piutti and his collaborators (4) found many years ago that hydroxides and alcoholates of alkali metals produced violet colors with unsaturated imides—for example, N-methyl maleimide, N-ethyl maleimide, and N-benzyl maleimide. It must be stressed, however, that the color reaction with thiols is several orders more sensitive than that with alcohols, so that interference by alcohols can be eliminated.

The new color reaction (5) provides an excellent means of visualizing sulfhydryl compounds on paper. It is especially suitable in connection with the systems for the separation of thioamino acids and peptides in the form of their NEM derivatives, which were described previously (6, 7). The main advantage of this method is the stabilization of the thiols during chromatography. However, since the usual color reactions for sulf-

hydryl groups are not given by the NEM complexes, ninhydrin had to be used to stain the chromatograms.

The new color reaction makes it possible to combine the advantage of protecting the sulfhydryl group during chromatography with that of visualizing the compounds by a reaction specific for this group. In this way, sulfhydryl-containing amino acids and peptides can be distinguished from other amino acids and peptides of the same  $R_f$ , which would not be possible with ninhydrin. Moreover, chromatography of thiols, as their NEM derivatives, can now be extended to thiols that do not contain an amino group. The following procedure is recommended for the visualization of thiols or thioesters.

Following chromatography by the methods described previously (7), the paper is dried thoroughly in a current of air. It is then dipped in a  $0.05M$  solution of NEM in absolute isopropanol. The paper is again dried in a current of air for 15 minutes, followed by dipping in  $0.25M$  potassium hydroxide (KOH) in absolute isopropanol. Pink to red spots appear immediately.

No color reaction is observed if the order of dipping is reversed or if a chromatogram treated with NEM is left to dry for 2 days before treatment with KOH. Isopropanolic solutions that contained higher and lower concentrations of NEM ( $0.1$  to  $0.025M$ ) and of KOH ( $0.5$  to  $0.125M$ ) were found adequate for dipping purposes. However, using the lower NEM concentration reduces the sensitivity of the method somewhat, whereas the higher concentration leaves a light pink background on the paper. This is undoubtedly caused by the Piutti reaction (4). In the case of NEM this background reaction is not observed with the recommended concentration, probably because of the volatility of this particular maleimide. On the other hand, a distinct red background is observed with N-phenyl maleimide, and the use of N-ethyl maleimide is therefore strongly recommended for paper chromatography.

The isopropanolic NEM solution was found to be stable for at least 8 days if it was stored in a dark glass container in the refrigerator. The color reaction was used successfully after chromatog-

raphy with the following solvent systems: isopropanol-formic acid-water, n-propanol-water, n-butanol-formic acid-water, isopropanol-ethanol-formic acid-water (7). Identical  $R_f$  values were obtained for compounds containing both an amino and a sulfhydryl group with NEM/KOH and with ninhydrin.

As little as  $1 \mu g$  ( $0.033 \mu mole$ ) of glutathione, or  $0.1 \mu g$  of sulfhydryl could be detected. Concentrations of this magnitude faded after a few hours. Higher amounts,  $3 \mu g$  and above, were stable for more than 48 hours. The color reaction was positive in solution and on paper with the following compounds: hydrogen sulfide, methyl mercaptan, ethyl mercaptan, amyl mercaptan, thioglycolic acid, ethyl thioglycolate, thioacetic acid, thiomalic acid, thiouracil, ergothioneine, cysteine, cysteinyl-glycine, glutamyl-cysteine, glutathione, coenzyme A; 2,3-dimercaptopropanol (BAL), lipoic acid, S-acetyl thioglycolic acid, S-acetyl glutathione, homocysteine thiolactone, and N-acetyl homocysteine thiolactone. Alcoholic solutions of ovalbumin also gave a pink color with NEM and alkali.

It is particularly interesting that bacitracin gave a positive reaction, since this peptide fails to show any of the common tests for sulfhydryl groups except after hydrolysis (8). No color reaction was obtained with the following: glycine, glutamic acid, glutamine, tyrosine, alanine, serine, aspartic acid, asparagine, valine, methionine, threonine, tryptophan, phenylalanine, dihydroxyphenylalanine, proline, cystine, homocystine, cystinyl-diglycine, diglutamyl-cystine, or oxidized glutathione (GSSG).

This reaction should serve as a useful tool for distinguishing and detecting sulfhydryl compounds, especially those in which the thiol group is the only functional group in the molecule. This is illustrated by our experience with some preparations of cysteinylglycine, which were found by this method to contain mercaptan impurities that do not give a ninhydrin reaction.

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- \* Special Public Health Service research fellow of the National Heart Institute.
- 7 December 1955

## Radioactivity in Thyroid Glands Following Nuclear Weapons Tests

Radioactivity has been reported (1) and confirmed (2) in the thyroid glands of cattle, presumably from  $I^{131}$  fallout. The present report (3) is a continuous study of the radioactivity in thyroids from the United States, Canada, England, Germany, and Japan during the past year. There was a series of 14 nuclear tests in Nevada from 18 February to 15 May 1955 and a test in the eastern Pacific Ocean in mid-May 1955 (4). Additional sources of fission products were presumably released by other countries in the winters of 1954 and 1955.

Dunning (5) has estimated biological ingestion of iodine fission products beginning 50 hours after fission results in more than 80 percent of the total radiation dose to the thyroid being due to  $I^{131}$ . When ingestion begins later,  $I^{131}$  rapidly becomes a more dominant iodine isotope. In the present investigation (6) all the radioactivity reported in thyroid glands will be considered as  $I^{131}$ .

The simple counting methods described previously (1) were used, except that after June 1955 all samples that contained less than 0.002  $\mu\text{mc/g}$  were tested in a 1½ by 2-in. NaI(Tl) well crystal in conjunction with a pulse height analyzer to increase accuracy in the determination. All samples were counted with a coefficient of variability (7)  $\pm 5$  to 12 percent, except those between October 1954 and June 1955 that contained less than 0.01  $\mu\text{mc/g}$ ; in these the coefficient of variability was  $\pm 30$  to 50 percent. The instruments were calibrated daily against an  $I^{131}$  standard. The well crystal with pulse height analyzer had a background of 0.12 count/sec and 1  $\mu\text{c}$   $I^{131}$  counted 6600 count/sec.

Human thyroids from all available autopsies in Memphis were tested, and the results from all 175 glands have been shown in Fig. 1. Thyroids from 15 unselected slaughterhouse cattle raised within 200 miles of Memphis were tested each week for 70 weeks. During the period of greatest radioactivity five to ten thyroids were received by airmail every 1 or 2 weeks from England, Ger-

many, Canada, Washington State and every 2 or 3 weeks from Japan. The radioactivity of these glands showed standard deviations similar to those from Memphis; therefore, for simplicity, only the average values for the foreign glands have been presented. The radioactivity was corrected for decay during the 4 to 10 days spent in transportation. The millimicrocuries per gram were plotted against the date of slaughter and bar graphs (Fig. 2) were constructed from these curves. Only the data for the first and 15th of each month are included in Fig. 2, and no bar is shown for an area unless there was a sample within 1 week of the date.

On 17-19 April 1955 the gamma radioactivity in the thyroid area was determined *in vivo* in 20 persons (USPH monitors and their families in Utah and Nevada). Most of these subjects were men stationed around the nuclear weapons tests site. Their work was to determine fallout patterns. A scintillation crystal was placed against the thyroid areas of their necks, and the results were compared with determinations over the thigh. Precautions were taken to prevent errors owing to surface contamination. The limit of sensitivity of these *in vivo* determinations was 2  $\mu\text{mc}$   $I^{131}$ . The results showed that only two individuals (men) had detectable amounts of radioactivity in their thyroid areas, and each of these has a total gamma-emitting equivalent of approximately 5  $\mu\text{mc}$   $I^{131}$ .

The relationship between total chemical iodine and radioactive iodine in cattle thyroids was investigated by analy-

ses of 20 glands with greatest extremes in  $I^{131}$  content. These showed no correlation between  $I^{127}$  and  $I^{131}$  content.

Figure 1 summarizes the most complete data. The ordinate is plotted on a 5-cy log scale in order to show early increases from the base line and also include the maxima, 10,000 times greater. The maximum value in any sample group was frequently 10 times greater than the minimum collected at the same time. Yet, every time the average value increased above 0.002  $\mu\text{mc/g}$ , the minimum was observed to increase. This suggested that the minimum intakes were possibly due to some mechanism, such as respiration, common to all the animals. The maximum values may be dependent on additional variable factors, such as ingestion of fallout material.

The increases shown in October 1954 to 15 February 1955 and November 1955 to March 1956 were believed to be due to nuclear tests, which, so far as I am aware, were not conducted by the USAEC.

Five days after the first test of the Nevada series, there was a detectable increase in the  $I^{131}$  content of cattle thyroids in Memphis. The minimum was above minimum detectable level and did not return to that level for 8 months. The observed rate of increase of thyroid  $I^{131}$  may be sensitive to the frequency of sampling and the freedom permitted the animal 2 or 3 days preceding slaughter. Two weeks elapsed between the beginning of the Nevada series and the first maximum of that period. The last maximum, 6 June, was observed 3 weeks after

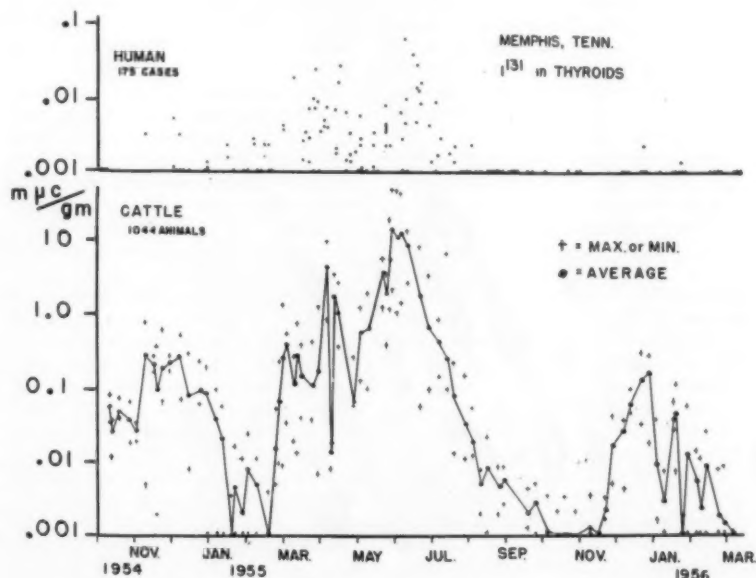


Fig. 1. Iodine-131 in human and cattle thyroid glands.

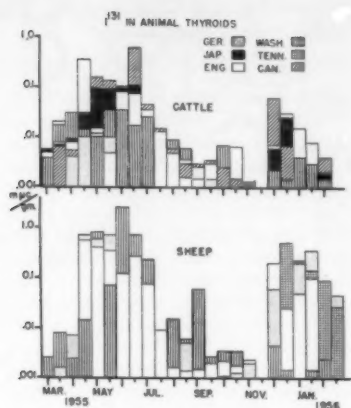


Fig. 2. Iodine-131 in cattle and sheep thyroid glands.

the last test of 15 May. The delay of 5 days to first detect radioactivity and 14–20 days to reach a maximum could suggest that a major fraction of the  $I^{131}$  fell out slowly (2). An additional explanation is the possibility that the environment was maximally "labeled" with  $I^{131}$  when the increase of thyroid  $I^{131}$  began. The thyroid gradually accumulated the isotope, but the  $I^{131}$  continually decayed. The result would be a rapid increase, since accumulation rate exceeded decay rate, then finally, decay rate would surpass accumulation, since the environmental intake and accumulated material both decayed.

At least the following 12 factors of unknown relative importance determined the maximum accumulation of  $I^{131}$  in thyroids distant from the test site: (i) total mass of  $I^{131}$  released, (ii) altitude of release and dust present, (iii) proportion of  $I^{131}$  or parent isotope released in gas and solid state, (iv) repeated nuclear tests, (v) distance the  $I^{131}$  traveled before detection in the thyroid gland, (vi) a flattening of the distribution curve of the radioactive concentration as the radioactive mass was diluted, (vii) weather conditions, (viii) possibility of radioactive mass returning to sample area after once passing, (ix) radioactive decay, (x) inadequacy of samples, (xi) continued intake of the isotope, (xii) rate of thyroid accumulation and release of the iodine.

The upper portion of Fig. 1 shows that  $I^{131}$  increased in human thyroid glands in Memphis when an increase was demonstrated in cattle. The maximum  $I^{131}$  per gram of human thyroid was less than 0.5 percent of the maximum for cattle from the same general area. This difference may be related to the fact that the human thyroid is more than 10 times larger than that of cattle (compared on

body weight basis), but the total volume of air inhaled per day is less in the human beings. In addition, human beings do not ingest large amounts of dust in their diet.

Figure 2 shows that increases in  $I^{131}$  content of thyroids from sheep in England and Germany occurred 2 to 4 weeks after the 1 March maximum in Memphis. These delays may have been due in part to factors ii, v, vi, vii, and x. The April maximum radioactivity in the samples from England and Germany was quantitatively similar to the March maximum in the Memphis cattle.

In areas from which both sheep and cattle specimens were obtained, if the  $I^{131}$  of one species exceeded the other, the sheep were consistently the greater. This may be related to ingestion of more dust by the close-grazing sheep.

The greatest concentration of  $I^{131}$  in Memphis specimens, 1 June, did not appear to be the season's greatest concentration outside of North America. The differences between the world-wide distribution of the March and June maximum may have been related to factors i, ii, vii, and x. In the spring of 1955 the distribution of  $I^{131}$  may have been relatively uniform throughout the entire Northern Hemisphere.

Dunning (5) has shown theoretical methods to estimate radiation dose from radioiodine fallout. Assuming that the 1044 cattle in Fig. 1 are representative, these data make it possible to determine experimentally the radiation dose in cattle of the Memphis area. The maximum and average data of Fig. 1 were plotted on square coordinates and the curves were integrated. The result was millimicrocuries per day per gram and this was multiplied by 12.3 (mrep per day per millimicrocurie of  $I^{131}$  per gram). The data for the Memphis cattle were studied by these analyses. The November 1954 fallout delivered a maximum of 0.30 rep and an average of 0.11 rep to the cattle thyroids; the Nevada series resulted in a maximum of 13 rep and an average of 4.3 rep in cattle thyroids; the fallout in the winter of 1955–56 produced a maximum of 0.10 rep and an average of 0.04 rep in the bovine glands.

Dunning's analysis applied to the Memphis cattle data on the last test of the Nevada series (15 May) showed an average of 4 to 6 rep delivered to the cattle thyroids. This equals the 4.3 rep, average calculated here for the entire Nevada test period.

The data from England (253 glands) were the most complete of those from outside the United States, so the average radiation was calculated for cattle and sheep in England during the period April–November 1955. This estimate showed 0.15 rep and 0.40 rep per thy-

roid for cattle and sheep, respectively, among the specimens from England. This radiation dosage can be compared with the 5000 to 10,000 rep from  $I^{131}$  necessary to treat hyperthyroidism in human beings.

Even though  $I^{131}$  fallout was easily detected in cattle and sheep thyroids the total radiation dose to the gland was small during the period studied.

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5 April 1956

#### Gum Replica Technique for Electron or Light Microscopy

In a study of the effects of organic solvents on the surface structures of plant-rust spores, the need arose for use of replica techniques in order that surface changes on the spore could be observed with the electron microscope. Replica techniques involving the use of heat, pressure, or organic solvents could not be utilized because of the sensitivity of spores to these treatments. Attempts to make replica patterns of rust spores by evaporation of silicon monoxide, carbon [D. E. Bradley, *Brit. J. Appl. Phys.* 5, 65 (1954)], and similar substances were unsuccessful, because the relatively large

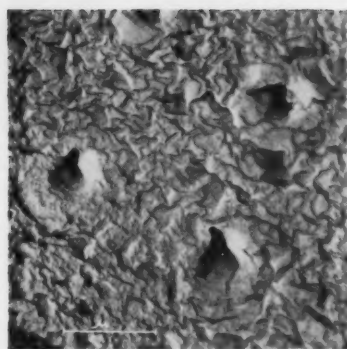


Fig. 1. Two-stage replica of a spore of wheat-stem rust that was obtained by using gum acacia and collodion. The replica is shadowed with uranium at a slope of 1:2. The surface is covered with wrinkles that are as high as  $0.2\ \mu$ . Spines averaging  $0.5\ \mu$  in height are spaced at intervals of about  $2\ \mu$ . The size and shape of these spines may be verified by examination of the periphery of the spore itself in the electron microscope.

size of the spores ( $15$  by  $30\ \mu$ ) prevented the formation of an even layer with the necessary thickness and strength. When the specimen was rotated through  $360^\circ$  during evaporation, the afore-mentioned replicating materials enveloped the particles and prevented their removal from the film.

The usual two-step replica process using gelatin or methyl cellulose in water for the negative, and collodion for the positive, replica was generally not successful. The primary reason for this difficulty is the absence of control over the depth of the negative replica. For instance, if rust spores, which are usually elliptical in cross section, are allowed to sink to a depth greater than one-half of the minor axis, the opening, through which the spore must pass if it is to be removed, will have a diameter smaller than the length of the major axis and prevent removal of the spore from the replica material. If the replica technique is to be consistently successful, the depth of the negative replica or impression must be controllable within narrow limits. It was this requirement that led us to develop a replica technique that employs gum acacia. It has proved successful for spores of *Bacillus subtilis* and stem rust of wheat. The technique may be described as follows.

1) A saturated solution of gum acacia in water, containing a small amount of formalin to retard spoilage, is filtered through a medium sintered-glass filter or its equivalent.

2) A glass slide is coated by being dipped into the gum solution. Care must be taken to prevent the formation of bubbles on the surface of the slide in this

procedure. The slide is then dried in a vacuum desiccator. Slides may be kept indefinitely and used as needed for routine samples.

3) The dry specimen is spread evenly over the gum surface, and the excess is shaken off by tapping the slide.

4) The slide is held face-down over warm water until a thin layer of gum is liquefied by the moisture. Both the temperature of the water and the exposure time may be adjusted to modify the extent to which the specimen penetrates the gum. Fifteen seconds' exposure  $1$  in. above water at  $50^\circ\text{C}$  gave good results with rust spores, while the best exposure time for bacterial spores was found to be  $5$  seconds. In each case only a small, relatively flat portion of the surface of the specimen formed an impression.

5) The slide is dried thoroughly in a desiccator, after which the specimen is brushed from it with cotton or cheesecloth. The hard surface of the gum is not damaged by this treatment, and the cloth does not actually strike the negative replica surface, which is visible as a depression with the light microscope. Examination at suitable magnification will indicate whether an adequate negative impression has been made and whether the specimen has been removed from the impression.

6) The slide with the negative gum replica is immersed in  $1$  percent collodion in amyl acetate and dried. The collodion is scored into small squares with a needle, and the slide is immersed in water to dissolve the gum and free the collodion. The positive collodion replica is caught face-up on a  $200$ -mesh specimen screen, shadowed with uranium, and examined in the microscope.

Removal of the specimen from the gum slide by brushing is practical in the formation of replicas of particulate matter larger than about  $0.5\ \mu$  in diameter. Smaller objects of nonbiological materials may be removed by being dissolved in a suitable solvent that will not etch or distort the gum. The gum technique has been the only means by which we have been able to make a replica of plant rust spores or bacterial spores without the disadvantages brought about by techniques that employ heat, pressure, or organic solvents. The gum was found to yield replicas of polystyrene latex particles with no demonstrable distortion. A resolution of better than  $200\ \text{\AA}$  was obtained. Figure 1 shows a positive replica of a spore of wheat-stem rust and indicates the surface detail that the method is capable of reproducing.

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1 December 1955

## Action of $p$ -{Di(2-chloroethyl)}-amino-L-phenylalanine on Harding-Passey Mouse Melanoma

Bergel and Stock have reported (1) an almost complete carcinostasis against the Walker rat carcinoma as a result of injecting  $p$ -{di(2-chloroethyl)}-amino-L-phenylalanine  $1$  day after implantation of the tumor. It seemed of interest to investigate the activity of this compound against mouse melanoma, partly because of the known resistance of the melanomas toward mustards, other chemotherapeutic substances, and x-rays (2). It will also be noted that the compound in question is a derivative of phenylalanine—an amino acid that serves as the ultimate precursor of the melanin that is so actively deposited by the melanocyte. From what is known of the phenomenon of metabolic antagonism, investigation of a phenylalanine derivative as a possible cytostatic agent against melanoma would seem to be worth while, even though the opinion is widely held that melanin formation is independent of the basic and vexing problem of tumor growth.

The experiments reported here were carried out on the Harding-Passey melanoma in dba, line 1, mice (3). The compound investigated was synthesized by the method of Bergel and Stock (4, 5). Resolution was achieved through the brucine salt of N-acetyl- $p$ -nitro-DL-phenylalanine, an advanced intermediate in the synthesis.

Thirty female dba mice,  $7$  to  $8$  weeks of age, were implanted on  $8$  October with the Harding-Passey melanoma from donor mice originally implanted  $3$  weeks earlier. The mice, then weighing about  $14$  g each, were divided by random selection into three groups, A, B, and C, of ten each.

On  $9$  October the mice of group A were injected intraperitoneally with the nitrogen mustard suspended in peanut oil. Each animal received  $0.4$  mg in  $0.4$  ml of peanut oil. By the fifth day it became apparent, despite the indications of preceding toxicity experiments on other mice, that this was virtually a lethal dose.

On  $17$  October the mice of group B were beginning to show very small tumors that could be discerned by palpation. On this date ( $9$  days after implantation) each mouse was injected intraperitoneally with  $0.2$  mg of the nitrogen mustard suspended in  $0.4$  ml of peanut oil (6).

On  $1$  November six mice selected at random from group B (all ten were alive) and six from group C were sacrificed. The tumors were excised and weighed. The tumors of the B group were uniformly small and weighed on the average  $0.028$  g each; those of the C mice were slightly more variable in

size but, in all cases, were much larger than the B-mouse tumors and weighed an average of 0.678 g each.

The mice of group B, with average tumor weights of 0.028 g when they were sacrificed, weighed, on the average, 14.3 g on implantation, 16.4 g on the fifth day (22 October) after injection of nitrogen mustard, and 17.5 g on the day before they were sacrificed (31 October). The control mice of group C, with average tumor weights of 0.678 g when they were sacrificed, weighed, on the average, 14.3, 17.0, and 17.7 g on 8 October, 22 October, and 31 October, respectively.

Although the findings strongly suggest that the single dose of 0.2 mg of the nitrogen mustard achieved a complete cessation of growth of the implant, experiments have yet to be performed to determine whether actual regression of a tumor of appreciable size can be achieved and whether the small static tumors of the B mice are viable.

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5. I am indebted to F. Bergel and J. A. Stock for their kindness in providing reference samples of the DL-, D-, and L-forms of the compound and to Howard Smith for synthesizing quantities of the DL-mixture and the L-isomer. Sally Williams and John Zemp assisted with the implantations and the injections. This work was carried out with assistance from the Cancer Institutional Grant, administered by Stanford University on behalf of the American Cancer Society.
6. This dosage approximates 14 mg/kg body weight.

16 November 1955

#### Increased Frequency of Births in the Morning Hours

It is generally felt that the incidences of day and night births are practically identical. Supporting this feeling is Guthmann's paper on the subject in which he combined 26,707 cases of his own with 95,087 culled from earlier literature (1). The resulting 121,794 cases showed that 49.1 percent of the births occurred during the day (6 A.M. to 6 P.M.) and 50.9 percent at night (6 P.M. to 6 A.M.).

The results reported here show a similar ratio between day and night—49.9 and 50.1 percent, respectively, among 33,215 births; but such an artificial division of the day into two 12-hour periods

distorts the picture entirely. By dividing the day into hourly periods, and tabulating the births for each hour, one finds a very marked and statistically significant peak in the morning hours. Using his own cases, Guthmann also found a peak in the morning hours, but this finding seems to have been neglected.

Excluding Caesarian section, second or third twins, and mid- and high-forceps delivery, human births at five hospitals in three different cities were classified by time of delivery. There were 33,215 such births: 8760 from the Edward W. Sparrow Hospital, Lansing, Mich., during a 3-year period; 2532 from the St. Lawrence Hospital, Lansing, during a 1-year period; 10,546 from the W. C. A. Hospital, Jamestown, N.Y., during an 8-year period; 9421 from the Jamestown General Hospital during a 9-year period; and 1956 from the Warren (Pennsylvania) General Hospital during a 2½-year period.

The 8 consecutive hours of greatest frequency of birth, the 8 consecutive hours of lowest frequency of birth, and the 8 remaining hours were compared with one another. Thus, three statistical populations were established, and the means were compared. Such comparison was made for each of the five hospitals individually, and for the total.

Combining the data from all five hospitals (Table 1) and using the formulas

$$\frac{S.D.}{\sqrt{8}} = \text{Standard deviation of mean (1)}$$

and

S.D. of difference between means =

$$\sqrt{(S.D. \text{ mean}_1)^2 + (S.D. \text{ mean}_2)^2} \quad (2)$$

gave the following results. (i) There was a mean of 1561 births (S.D. 47) for each hour during the peak hours of 3 A.M. to 11 A.M. (ii) There was a mean of 1213 births (S.D. 66) for each hour during the low hours of 3 P.M. to 11 P.M. (iii) There was a mean of 1375 births (S.D. 65) for each hour during the remaining hours of 11 A.M. to 3 P.M. and 11 P.M. to 3 A.M. (iv) During the peak hours, 28.7 percent more births occurred than during the low hours. The standard error of the difference of the means of the two groups was 28; hence the difference is extremely significant statistically (12  $\sigma$ ), the odds being 1 in approximately  $6 \times 10^{28}$  that this difference is due only to chance. By taking three standard deviations of the difference between the means of the peak and low hours, one obtains a meaningful range of 21 to 36.9 percent. (v) The peak hour was 5 A.M.; it showed 48 percent more births than the low hour of 7 P.M.

Analysis of the data from each hospital individually was even more striking than the analysis of the total. Each of the five

Table 1. Number of births each hour of the day in five hospitals.

Time	No. of births
<b>Group A (3 A.M. to 11 A.M.)</b>	
3	1590
4	1560
5	1632
6	1547
7	1470
8	1588
9	1585
10	1515
<b>Group B (11 A.M. to 3 P.M. and 11 P.M. to 3 A.M.)</b>	
11	1422
12	1418
1	1480
2	1416
11	1355
12	1297
1	1281
2	1335
<b>Group C (3 P.M. to 11 P.M.)</b>	
3	1134
4	1276
5	1180
6	1213
7	1103
8	1267
9	1298
10	1253

hospitals showed a statistically significant difference between the means of the 3 A.M.-to-11 A.M. and the 3 P.M.-to-11 P.M. periods. The number of standard deviations in each group is as follows: (i) Sparrow Hospital, 11  $\sigma$ ; (ii) St. Lawrence Hospital, 4.5  $\sigma$ ; (iii) Warren General Hospital, 3.25  $\sigma$ ; (iv) W. C. A. Hospital, 7  $\sigma$ ; (v) Jamestown General Hospital, 10  $\sigma$ .

By taking the odds in each of these five and multiplying them together, one can estimate that the likelihood of the differences between the peak and low groups being due to chance is 1 in about  $10^{60}$ .

I did a similar analysis of Guthmann's 26,707 cases and found that the period from 2 A.M. to 10 A.M. showed 7.8 percent more births than the period from 2 P.M. to 10 P.M. This difference was statistically significant (4  $\sigma$ ) and, although it is not great, it tends to corroborate the findings presented here. The periods are not identical with mine because Guthmann's cases were tabulated in periods of 2 hours.

To argue that there are "only 33,215" cases here and hence not enough to prove the point is to ignore the fact that each of the five hospitals alone showed similar peak and low hours that were statistically significant. The same results in many smaller groups are more significant than a certain result in one large group.

It may be felt that the inclusion of low-forceps deliveries disguises the true situation. However retabulation of the 10,546 W. C. A. Hospital cases showed the same

statistically significant peak and low hours in both the 5039 spontaneous and the 5507 low-forceps deliveries, just as was seen in the total for each hospital and in the grand total.

It is interesting that Charles (2) and also Guthmann (1) noted a daily disproportion in the frequency of the onset of labor. Charles found that 62 percent of labors began between 9 P.M. and 9 A.M., the midpoint of this period being 4 hours before the midpoint of the peak period of birth given here.

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9 November 1955

### Adrenal Cortex and the Parotid Secretion of Sodium-Depleted Sheep

The isolation of aldosterone (1) has stimulated inquiry into the role of the adrenal gland in the changes occurring in the activity of electrolyte-secreting tissues as a result of sodium ion ( $\text{Na}^+$ ) depletion (2). The necessity of adequate techniques of bioassay has been emphasized accordingly (3).

It has been reported elsewhere (4) that sheep with a modified Pavlov-Glinski fistula of the parotid duct lost 2 to 4 lit of hypertonic alkaline saliva each day (composition:  $\text{Na}^+$ , 170 to 180 mequiv/lit;  $\text{K}^+$ , 5 to 15 mequiv/lit;  $\text{Cl}^-$ , 8 to 15 mequiv/lit;  $\text{HCO}_3^-$ , 120 to 150 mequiv/lit;  $\text{HPO}_4^{--}$ , 15 to 40 mequiv/lit;  $\text{Na}^+/\text{K}^+ = 18$  to 25). If the fistula loss of  $\text{Na}^+$  was not replaced, these sheep became rapidly depleted of large quantities of  $\text{Na}^+$ , and the  $\text{Na}^+/\text{K}^+$  ratio of the saliva decreased commensurately

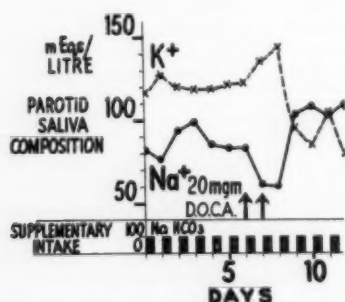


Fig. 1. Parotid fistula No. 7. Effect of DOCA on electrolyte composition of parotid saliva of a sheep moderately depleted of  $\text{Na}^+$ .

from 18 to 0.1. Since the  $\text{Na}^+ + \text{K}^+$  total remained virtually constant, and the anion pattern was little changed, the saliva retained its hypertonicity and alkalinity.

At the outset, a tentative hypothesis was that the change in  $\text{Na}^+/\text{K}^+$  ratio was mediated by the activity of the adrenal cortex, responding in some way to  $\text{Na}^+$  depletion by enhanced production, presumably of aldosterone, which in turn affected the electrolyte output of the sheep's parotid gland. The following experiments were carried out (5).

Desoxycorticosterone (DOCA) was administered to a normal sheep with a parotid fistula. The animal, which had been moderately depleted of  $\text{Na}^+$  during the previous 15 days, was secreting saliva of altered pattern ( $\text{Na}^+$ , 76 to 100 mequiv/lit;  $\text{K}^+$ , 115 to 128 mequiv/lit). On 2 successive days 20 mg of DOCA was injected intramuscularly, and a definite alteration of salivary  $\text{Na}^+/\text{K}^+$  ratio resulted (Fig. 1). If, however, the same dosage of DOCA was given when the animal was grossly depleted of  $\text{Na}^+$  (salivary pattern  $\text{Na}^+/\text{K}^+ = 30/170 = 0.18$ ), there was less than 5 mequiv/lit effect on the concentrations. Thus DOCA was shown to produce an effect on the salivary electrolyte pattern. But was the adrenal cortex the regulator of the change seen during  $\text{Na}^+$  depletion?

Sheep with unilateral parotid fistulas were bilaterally adrenalectomized.

1) If adequate  $\text{Na}^+$  replacement was given, the sheep could be maintained in good condition indefinitely on a daily dose of DOCA (5 to 10 mg) and cortisone (25 mg). DOCA was the more critical component. The volume and electrolyte pattern of parotid saliva were normal.

2) If adrenal-hormone supplement alone was withdrawn, the usually observed fall in plasma  $\text{Na}^+/\text{K}^+$  ratio and large  $\text{Na}^+$  loss in the urine occurred (Fig. 2). However, despite the negative  $\text{Na}^+$  balance (136 mequiv), there was no characteristic fall in the salivary  $\text{Na}^+/\text{K}^+$  ratio. In fact this ratio rose (Fig. 2). The animal's condition rapidly deteriorated. When the adrenal hormones were replaced, the salivary  $\text{Na}^+/\text{K}^+$  ratio fell to a level consistent with the existing degree of  $\text{Na}^+$  depletion.

3) If the DOCA supplement was increased (40 mg/day), the salivary  $\text{Na}^+/\text{K}^+$  ratio fell from 17 to 2.0 in 5 days.

4) If  $\text{Na}^+$  replacement was withheld, and the usual maintenance-hormone supplement continued, a state of adrenal insufficiency developed within 2 to 4 days. Despite the  $\text{Na}^+$  depletion, there was little or no change in the salivary  $\text{Na}^+/\text{K}^+$  ratio.

5) If, however,  $\text{Na}^+$  was withdrawn during a period of constant but increased

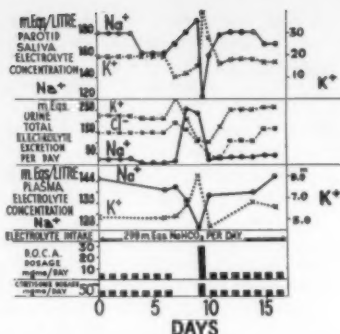


Fig. 2. Adrenalectomy No. 1. Effect on parotid saliva, urine, and plasma of withholding DOCA and cortisone from a bilaterally adrenalectomized sheep with a parotid fistula. The daily  $\text{Na}^+$  supplement was given throughout the experiment.

DOCA dosage (20 mg/day), the salivary  $\text{Na}^+/\text{K}^+$  ratio fell to that seen during  $\text{Na}^+$  depletion in a nonadrenalectomized sheep. Figure 3 shows that the increased DOCA dosage lowered the salivary  $\text{Na}^+/\text{K}^+$  ratio, and that an equilibrium state was reached before the  $\text{Na}^+$  withdrawal. The pattern returned to this equilibrium ratio upon restoration of  $\text{Na}^+$  balance. Hence, adrenal steroids do alter the sheep's salivary electrolyte pattern, and it is a necessary condition that they be provided in excess of basal-maintenance dose if this electrolyte pattern is to vary commensurately with  $\text{Na}^+$  depletion as in a normal animal.

However, the finding in item 5 of an unequivocal response to  $\text{Na}^+$  depletion on a constant DOCA dosage suggests that the "cause" of this parotid behavior in the normal animal is the simultaneous interaction of at least two factors. Probably the adrenal secretion is one contributory condition in a set of jointly

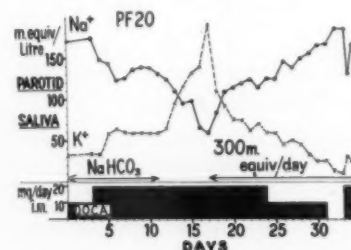


Fig. 3. Parotid fistula No. 20.  $\text{Na}^+$  depletion (515 mequiv) in a bilaterally adrenalectomized sheep with a parotid fistula.  $\text{Na}^+$  depletion caused a clear-cut fall in the  $\text{Na}^+/\text{K}^+$  ratio of parotid saliva, in addition to that caused by increased DOCA dosage. After the recovery period, DOCA alone was withheld for 2 days (days 31 and 32) and, in this circumstance, the  $\text{Na}^+/\text{K}^+$  ratio of saliva rose, despite a negative  $\text{Na}^+$  balance of 300 mequiv.

sufficient and severally necessary conditions, and it would seem more correct, in this situation, to describe its role as such, than as permissive of the action of other factors. Lorenz (6), in analyzing innate behavior patterns, has used Erlich's term *amboceptor* in like circumstances.

The value of this preparation is that the electrolyte activity of adrenal steroids can be examined in a conscious animal in normal correspondence with its environment at strictly controlled levels of  $\text{Na}^+$  depletion.

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- 12 March 1956

### Cholinesterase Activity of Human Leucocytes

The erythrocytes and the serum of blood are known to possess cholinesterase activity, but the experiments of Fegler, Kowarszyk, and Szpunar (1) have been generally accepted (2) as proof of the absence of cholinesterase in the white blood cells of man. Hines (3) also reports that he was unable to find cholinesterase activity in the white layer of centrifuged human blood, but he gives no details. We wish to report here experimental evidence that human leucocytes contain appreciable amounts of an acetyl- $\beta$ -methylcholine chloride (Mecholyl) (4) splitting enzyme.

White-cell preparations were obtained from the blood of seventeen young, apparently healthy males. The method of separation selected was the flotation technique of Vallee, Hughes, and Gibson (5), with the exception that the flotation solution was made up with dextran instead of the albumin used by these authors. Cholinesterase activity determinations were performed according to a modification of the electrometric method of Michel, (6), in which the cleavage of Mecholyl identified the white-cell enzyme as being similar to the cholinesterase of

erythrocytes and brain tissue (7). The use of this substrate also obviated the necessity for complete removal of residual plasma from the preparations.

Concomitant determinations, using Mecholyl, of the erythrocyte cholinesterase activity were performed on each sample of whole blood for purposes of comparison. Hematocrit determinations permitted the activity values to be expressed in terms of a unit volume of packed cells, thus compensating for variations in the total packed red-cell volume.

The flotation solution was made up by first dissolving 214.2 g of sodium chloride-free clinical dextran (8) in 900 ml water. Then 0.6092 g of solid sodium chloride was added to 100 ml of the dextran solution to give a freezing-point depression of  $0.57^\circ\text{C}$  and a specific gravity of 1.079. This solution is isotonic with plasma and has a density that is intermediate between the densities of the normal erythrocyte and leucocyte.

For each determination, 15 ml of freshly drawn heparinized blood was carefully layered onto 10 ml of dextran solution in a 40-ml test tube having an inside diameter of 25 mm. The tube was centrifuged for 10 minutes at 42 g and then for 20 minutes at 1500 g. The plasma was drawn off and the white cells that had collected at the dextran-plasma interface were pipetted into a graduated 15-ml centrifuge tube. The volume was increased to 5 ml by the addition of isotonic saline, and the cells were homogeneously suspended by inversion.

A Van Allen microhematocrit tube of known total volume and with a calibrated stem was filled to the new calibration mark above the bulb with an aliquot of this suspension and was centrifuged at 1400 g for 10 minutes. Some cells usually adhered to the sloping sides of the upper part of the tube; these were freed from the wall with the aid of a thin piece of wire. The tube was then returned to the centrifuge and was spun for an additional 20 minutes. In this way, values for white-cell concentrations were obtained that were expressed in terms of volume of packed white cells per unit volume of suspension. Microscopic examination of stained smears of the packed cells showed that contamination by erythrocytes was negligible.

The remaining portion of the white-cell suspension, of known volume and leucocyte concentration, was packed in the centrifuge tube by spinning for 5 minutes at 360 g. The cells were resuspended in 0.5 ml of saline and transferred undiluted to a 5-ml beaker for the electrometric activity determination. To the leucocyte suspension (or to 0.02 ml of whole blood in 0.5 ml of water) was added 0.5 ml of Michel's buffer No. 2 (9), followed by 0.1 ml of 0.22 F Me-

cholyl (10). The initial pH reading was made immediately, using a model G Beckman pH meter equipped with glass and calomel electrodes. The beaker was then placed in a water bath at  $25 \pm 1^\circ\text{C}$  for 1 hour, after which, the pH was again determined. All experimental pH differences were corrected for nonenzymatic hydrolysis by means of accompanying blank determinations. Hematocrits of the whole blood were determined in Win-trobe tubes by spinning at 1500 g for 30 minutes.

Triplicate determinations were performed on 3 successive days on four subjects in order to permit an evaluation of the analytic precision. Day-to-day variations were thus included in the measure of precision. There is a wide variation among the subjects in the values for white-cell cholinesterase, but the red-cell values fall within a narrow range, in agreement with previous results. The mean leucocyte-cholinesterase activity is  $0.028 \Delta \text{pH/hr mm}^3$  packed cells, with 95-percent confidence limits of  $\pm 0.016$ . The standard deviation of the triplicate analyses is  $\pm 0.014$  (coefficient of variation = 49 percent), which indicates the relatively low order of precision of the individual results. Application of the F test yielded a value exceeding the 1-percent point, from which it may be concluded that the method is sufficiently precise to detect differences from one individual to another. The mean value for erythrocytes is  $0.069 \Delta \text{pH/hr mm}^3$  packed cells (standard deviation =  $\pm 0.007$ ); the ratio of the mean activity of packed erythrocytes to the mean activity of packed leucocytes is then 2.5. Graphic comparison of the activities of the two cell types showed the absence of any systematic relationship between them.

This investigation adds another item to the long list of tissues that are known to contain cholinesterase. Further studies will be required to elucidate the function of this enzyme in the leucocytes.

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9. This is 0.006 formal in sodium barbital, 0.001 formal in  $\text{KH}_2\text{PO}_4$ , and 0.30 formal in NaCl. The pH is adjusted to 8.00 by the addition of 0.1 F HCl.

10. Concentrations are expressed in volume formality, F, the number of formula weights per liter of solution.

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25 November 1955

# Clinical Experiment on the Use of Sodium N-Lauroyl Sarcosinate in the Control of Dental Caries

The belief is widely held that dental caries is caused by acids formed on a tooth surface by the enzymic degradation of carbohydrates (1). On the basis of this concept, attempts have been made to control dental caries by reducing the availability of the sugar substrate (2), by making the tooth more resistant to acids (3) or by the prevention of fermentation. One method of control that has been suggested (4) makes use of enzyme inhibitors to prevent the glycolysis of the sugars. This method has been clinically tested with the use of a dentifrice containing 2-percent sodium N-lauroyl sarcosinate (5), a very effective inhibitor of hexokinase *in vitro* (6).

The test subjects were young adults from the Meredith Publishing Company, Des Moines, Iowa, and from the student bodies of the University of Miami, Florida, the University of Florida, Gainesville, and Drake University. The experiment at each geographic location was conducted independently by different investigators, although the procedures used were the same and were formulated by an over-all coordinator.

Each subject was classified in one of the following test groups. *T-1-D*: Subjects used a dentifrice containing 2-percent sodium N-lauroyl sarcosinate morning and night. *T-2-D*: The same dentifrice was used after each meal. *C-1*: Subjects used a dentifrice of their choice in the manner to which they were accustomed. *C-2-D*: Subjects used, morning and night, a dentifrice identical to that used by the *T-1-D* and *T-2-D* groups, except that sodium N-lauroyl sarcosinate was replaced by 2-percent sodium salt of sulfated glyceride of coconut fatty acids. In all groups except *C-1*, instructions were given for proper brushing techniques, and all subjects were issued dentifrice and brushes as needed.

Since it was expected that 30 to 40 percent of the participants in the experiment would drop out each year, the homogeneity of the groups was not determined until the experiment had been completed. Comparisons were made then from data collected before the tests among the various groups and locations in respect to distribution of age; sex; DMF (decayed, missing, filled) surfaces; DF teeth; missing teeth; caries-free surfaces; caries-free

teeth; free proximal surfaces; free labial, lingual, or buccal surfaces; and free occlusal surfaces.

At the start of the experiment, the average age of the subjects was 26 at Meredith, 19 at Drake, 22 at Miami, and 20 at Gainesville. In all groups and locations, the males were slightly more numerous than the females. Although within each group the numbers of decayed, missing, and filled surfaces were consistent, the counts were somewhat higher at Meredith and considerably higher at Gainesville. Initial examinations were

made on 2543 subjects. At the end of the first year of the test, there were 1883. This number decreased to 1159 subjects who completed the full 2 years of the experiment.

The increment of new carious surfaces was determined by clinical examination and radiographs, as was the involvement of teeth that had been noncarious at the start of the tests. In this regard, test subjects were compared with the controls with the data from each installation. Inasmuch as the group at Gainesville was not strictly comparable with the others

Table 1. Dental caries activity during 2-year test period.

Group	Installation	Condition at start		2-year increment of dental caries					
		No. subjects	Avg. age	Average no.		Teeth		Surfaces	
				DMF surfaces	DF teeth	$\bar{x}$	$\sigma^2$	$\bar{x}$	$\sigma^2$
C-2-D	Gainesville	41	20.2	51.6	19.7	0.76	0.49	7.51	14.55
	Miami	86	22.1	39.4	16.6	0.57	0.51	3.19	4.91
	Meredith	182	26.6	35.8	16.0	0.39	0.40	1.78	2.72
	Drake	74	18.8	34.1	16.2	0.38	0.43	1.69	3.04
	All groups	383	23.4	38.0	16.6	0.47	0.45	2.69	7.63
T-1-D	Gainesville	60	19.5	44.5	19.0	0.40	0.45	4.25	9.62
	Miami	107	21.5	37.3	16.0	0.18	0.25	1.12	2.09
	Meredith	116	26.7	37.1	16.3	0.15	0.16	0.68	0.95
	Drake	135	19.5	34.6	16.0	0.21	0.26	1.07	1.79
	All groups	418	22.0	37.4	16.5	0.22	0.26	1.43	4.10
T-2-D	Gainesville	36	20.3	55.9	20.1	0.50	1.00	4.22	15.22
	Miami	105	23.0	40.2	16.2	0.24	0.25	1.20	1.78
	Both groups	141	22.3	44.2	17.2	0.31	0.44	1.97	6.90
C-1	Gainesville	19	19.7	56.5	20.5	0.79	1.62	7.00	24.00
	Miami	82	22.1	34.6	15.4	0.62	0.83	2.71	5.48
	Meredith	86	26.6	35.0	16.1	0.44	0.48	1.92	3.18
	Drake	30	19.4	32.0	15.2	0.17	0.14	1.40	3.35
	All groups	217	23.3	36.4	16.1	0.50	0.68	2.60	7.82

Table 2. Comparison of control and test results.

Contrast	Installation	Teeth		Surfaces	
		Reduction (%)	t	Reduction (%)	t
C-2-D vs. T-1-D	Gainesville	47	2.62*	43	4.72†
	Miami	68	4.45†	65	7.82†
T-1-D	Meredith	62	3.67†	62	6.55†
	Drake	45	2.07*	37	2.88‡
	All groups	53	5.88†	47	7.40†
C-2-D vs. T-2-D	Gainesville	34	1.34	44	3.73†
	Miami	58	3.76†	62	7.65†
	Both groups	51	3.83†	57	7.03†
C-1 vs. T-1-D	Gainesville	49	1.74	39	2.90‡
	Miami	71	4.22†	59	5.75†
T-1-D	Meredith	66	3.78†	65	6.33†
	Drake	-24	-0.40	24	1.14
	All groups	56	5.33†	45	6.02†
C-1 vs. T-2-D	Gainesville	37	0.92	40	2.30*
	Miami	61	3.64†	56	5.55†
	Both groups	52	3.23‡	44	3.98†

\* Significant level 0.05. † Significant level 0.001. ‡ Significant level 0.01.

on the basis of oral conditions at the start of the experiment, the distribution between the test and control subjects was such that it was thought of interest to list each group separately in addition to indicating over-all results.

The results of the 2-year experiment are shown in Tables 1 and 2 and indicate that sodium N-lauroyl sarcosinate in a dentifrice, when it is used either morning and night or after meals, will materially reduce dental caries activity. The percentage reductions in Table 2 are average reductions for the test groups. Individual subjects may have derived more or less benefit than the average. The results from each group, with the exception of a small group at Drake and one at Gainesville, are highly significant, whether the comparisons are made on the basis of teeth involved or tooth surfaces involved.

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16 November 1955

#### Demonstration of Particulate Adhesion of the Rieckenberg Type with the Spirochete of Syphilis

In 1917 Rieckenberg (1) described an adhesion reaction between trypanosomes and blood platelets requiring antibody. Microorganism-antibody systems that are not trypanosomal have also shown this reaction, and particulate materials such as white cells, bacteria, and gamboe particles can substitute for platelets (2). The reaction, however, has been more difficult to elicit with the spirochete of syphilis, although Krantz in 1930 reported platelet adhesion to pathogenic *Treponema pallidum*, and Turner et al. observed that in treponeme-syphilitic serum mixtures tissue debris tended to stick to the organisms (3). Recently, doubt has been cast on the existence of the Rieckenberg phenomenon with the syphilis organism in a report of the fail-

ure to observe its adhesion with organic or inorganic particles (4). We wish to record our experience in being able to observe regularly the Rieckenberg type of adhesion with *T. pallidum* (5).

Suspensions of treponemes (Nichols strain) were separated from rabbit testes by the method of Hardy and Nell (6). The organisms, which were centrifuged from the citrate solution employed by these authors, were resuspended in fresh citrate solution, recentrifuged, drained carefully to remove the citrate, and finally resuspended and stored in sterile 0.85 percent sodium chloride solution. The temperature for the organisms was maintained at 4°C during each of these procedures.

Adhesion in the presence of serum was observed by dark-field microscopy. Involvement varied from an occasional treponeme to almost 100 percent, and the number of particles that adhered to different treponemes varied considerably. One particle or innumerable particles might be adherent to a treponeme. When the number of particles that adhered was small, the particles tended to accumulate at the tip of the treponeme. Treponemes to which many particles became attached were often difficult to distinguish.

Materials that were shown to adhere to treponemes were the following: *Streptococcus pyogenes*, *Streptococcus lactis*, *Escherichia coli*, *Alkaligenes fecalis*, *Spirillum rubrum*, *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, collodion particles, blood platelets (man, rabbit, guinea pig), and red-cell ghosts (sheep, rabbit, guinea pig, chicken). Blood platelets were collected by differential centrifugation from whole blood with 0.1 percent sodium ethylenediaminetetracetate (EDTA) and, for use in adhesion tests, were washed and resuspended in saline. The yeasts were least effective. *Streptococcus pyogenes* proved quite satisfactory. This organism, in saline, could be stored in an icebox for more than a month. However, the amount of adhesion to treponemes was sometimes increased by centrifugation and resuspension in fresh saline a few days or a week before use.

The adhesion did not occur with heat-inactivated rabbit and human serums in the absence of added guinea pig serum or when the added guinea pig serum was first diluted 10 times. Furthermore, either the application of heat or the addition of a chelating agent such as EDTA caused guinea pig serum to lose its capacity to support adhesion. The effect of the chelating agent was reversed by the addition of a mixture of calcium and magnesium ions. These cations themselves were inhibitory at high concentrations. These suggestions of a role for

Table 1. Comparison of adhesion reactions with standard serologic tests (STS) and treponemal immobilization tests (TPI) in 80 human serums.

STS	TPI	No. of serums	Adhesion reaction with streptococci*		
			+	±	0
+	+	12	12		
0	+	11†	6	1	4
+	0	7‡	1		6
0	0	13	1		12
+	Not done	26	26		
0	Not done	11	1§		10

\* Positive reaction (+) denotes more than 10 percent of 50 to 100 treponemes counted showing adherent cocci. Doubtful reaction (±) denotes adhesion consistently to about 10 percent of treponemes, usually with only one or two cocci adherent to one end of a treponeme. Negative reaction (0) denotes less than 10 percent adhesion.

† Eleven serums from old, treated cases of syphilis.

‡ Seven serums from clinically diagnosed biologic false positive (BFP) reactors.

§ This serum tested positive with *S. lactis* and negative with *S. pyogenes*.

complement are not unique, since others have previously implicated complement in the Rieckenberg reaction (7).

Serums from five rabbits that were infected with *T. pallidum* gave the adhesion phenomenon, while five normal rabbit serums did not. Reactions with human serums (Table 1) revealed a correlation of the adhesion reaction with traditional flocculation tests for syphilis and the treponemal immobilization test. These tests were performed by mixing 0.1 ml of serum with 0.1 ml each of guinea pig serum, saline, and saline suspensions of treponemes and cocci and then incubating the mixture at 34°C for 2 hours. As a control for each serum, in another tube guinea pig serum was replaced by saline. The stock suspension of cocci had a turbidity corresponding to the first tube of a MacFarland nephelometer, and the treponemes had a concentration of 80 million organisms per milliliter. Group A *S. pyogenes* (strain C203S) was employed except for 13 serums tested with *S. lactis* (ATCC7963).

The findings permit the conclusion that antibody responsible for adhesion is a result of *T. pallidum* infection. They do not define either the sensitivity or the specificity of the reaction. There also remains to be elucidated what roles the kinds of treponeme preparations and particles chosen for demonstrating adhesion may play in determining the specificity of the reaction.

Two antisera that were prepared against cardiolipin in presumably normal rabbits by A. G. Osler gave positive ad-

hesis reactions, suggesting that antibody to cardiolipin can participate in the adhesion. On the other hand, human syphilitic serums that were rendered negative to standard flocculation tests by absorption with cardiolipin remained adhesion positive, some of the absorbed serums showing a decrease in the degree of adhesion and others not. Also, some human serums from old, treated cases of syphilis that gave negative flocculation tests but positive treponemal immobilization tests showed adhesion. These observations probably indicate that more than a single antibody is capable of inducing adhesion.

The presence of antibody against bacterial indicator particles such as *S. pyogenes*, *S. lactis*, or *E. coli* did not interfere with adhesion to the treponemes. This was determined by comparison of adhesion with individual syphilitic serums before and after absorption with bacteria. A high-titer agglutinating rabbit antiserum against *E. coli* caused no adhesion between *E. coli* and *T. pallidum*, either with or without added guinea pig serum, and numerous non-syphilitic human serums that contained *E. coli* or streptococcal agglutinins did not cause adhesion of *T. pallidum* to the respective bacteria. Thus, while the bacteria can serve in the treponemal system, the treponemes do not seem to act readily as adhering particles in the bacterial antibody serums.

Nelson (4) has described as "immune adherence" a reaction involving a mixture of immune serum, human red cells, complement, and treponemes in which, presumably, adhesion is measured indirectly by the disappearance of treponemes from the suspension after centrifugation. This reaction was differentiated from the Rieckenberg phenomenon by Nelson on the basis of its occurrence only with human erythrocytes and its failure with platelets, white cells, charcoal, magnesium silicate, and suspensions of *Candida albicans*. In this connection, it is pertinent to recall the earlier work of English investigators (8) who labeled as "red cell adhesion" their observations of the regular ability of primate red cells to adhere to trypanosomes in the presence of complement and specific antibody. These workers and Raffel (9) found only an occasional rabbit, guinea pig, or rat that possessed erythrocytes capable of adhesion in the trypanosomal system, but they considered "red cell adhesion" to be an example of Rieckenberg adhesion. We have not seen unaltered sheep, rabbit, guinea pig, or chicken red cells adherent to *T. pallidum*, but these various kinds of cells, after lysis with distilled water, do yield ghosts that readily act as adhering particles. Our observations and the literature cited make it logical to conclude that "immune adherence" with human

red cells is simply a particular case of a general phenomenon—namely, adhesion of the Rieckenberg type.

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9 December 1955

### Duttonite, New Vanadium Mineral from Peanut Mine, Montrose County, Colorado

Duttonite,  $\text{VO}(\text{OH})_2$ , is a new mineral found in the Peanut Mine, Montrose County, Colo. (1). It is named in honor of Clarence Edward Dutton (1841–1912), who was one of the first geologists working in the Colorado Plateau region and who was a member of the U.S. Geological Survey from 1879 to 1891. The Peanut Mine is a vanadium-uranium deposit in the upper ore-bearing sandstone of the Salt Wash sandstone member of the Morrison formation of late Jurassic age. Ore bodies occur along the flanks of a buried channel and are localized by a crossbedding structure that is associated with the channels.

Most of the ore at the Peanut Mine is unoxidized, and the principal ore minerals are montroseite, paramontroseite (2), vanadiferous silicates, uraninite, and coffinite. The ore minerals impregnate sandstone and replace coalified wood. Along fractures in the ore-bearing sandstone there is commonly a thin massive coating of an undescribed vanadium oxide. On this coating duttonite occurs as crusts and coatings of randomly oriented, 6-sided platy crystals. The crystals range in size from extremely minute to

about 0.5 mm in the longest dimension. Associated minerals are melanovanadite and abundant crystals of hexagonal native selenium.

Duttonite is light brown and has a vitreous luster. The hardness is about 2.5. The calculated specific gravity is 3.24. The optical properties of duttonite indicate orthorhombic symmetry. It is biaxial positive;  $2V$  is about  $60^\circ$ ; and the dispersion is  $r < v$ , moderate.  $X = a$  (pale pinkish brown);  $Y = c$  (pale yellow brown);  $Z = b$  (pale brown);  $\alpha = 1.810 \pm 0.003$ ;  $\beta = 1.960 \pm 0.003$ ; and  $\gamma > 2.01$ . The optical properties of duttonite are very close to those of uvanite (3), but the two minerals differ both in composition and occurrence. Duttonite is an early oxidation product of montroseite ore, whereas uvanite ( $\text{U}_2\text{V}_2\text{O}_{21} \cdot 15\text{H}_2\text{O}$ ) occurs in highly oxidized ore.

The chemical analysis by one of us (R. M.) shows  $\text{V}_2\text{O}_5$ , 2.6 percent;  $\text{V}_2\text{O}_3$ , 75.3 percent;  $\text{FeO}$ , 0.4 percent;  $\text{H}_2\text{O}$ , 18.1 percent; and insoluble material, 4.2 percent; total, 100.6 percent. The chemical analysis confirms the formula  $\text{VO}(\text{OH})_2$  that was first arrived at through crystal structure determination (4).

The unit-cell constants of duttonite were measured by M. E. Mrose of the U.S. Geological Survey as follows: monoclinic,  $a_0 = 8.80 \pm 0.02$  Å,  $b_0 = 3.95 \pm 0.01$  Å,  $c_0 = 5.96 \pm 0.02$  Å,  $\beta = 90^\circ 40' \pm 5'$ . The space group is  $I 2/c$ , ( $C_{2h}^6$ ), the cell contents are 4  $\text{VO}(\text{OH})_2$ . The crystals are strongly pseudocubic, and the structure departs only slightly from the space group Imcm.

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#### References and Notes

1. Duttonite was found by one of us (C.H.R.) in the course of a study of the geology and mineralogy of the Peanut Mine as part of the program being conducted by the U.S. Geological Survey on behalf of the Division of Raw Materials of the U.S. Atomic Energy Commission. The publication of this paper was authorized by the director, U.S. Geological Survey.
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21 November 1955

### Lack of Recognition of Foreign Works

I have noted with increasing alarm a tendency of American scientists to practice a form of nationalism that scarce does credit to science. I refer to refer-

Table 1. References to foreign works by geologists from various countries.

Nationality	Books (No.)	Percentage frequency of references to foreign workers					
		10 (%)	11-20 (%)	21-30 (%)	31-40 (%)	41-50 (%)	51 (%)
American	100	75	18	5	2		
British	100	11	36	33	9	5	6
German	50	8	54	18	8	4	8
French	50	10	24	30	18	4	
Dutch	50	4	8	16	8	16	48
Swiss	50	14	12	18	22	14	20

ences made in publications that show an amazing lack of recognition of foreign works. Admittedly on a national population basis, America likely has more scientists than other nations, but then we are not concerned with mere quantities.

I have gone carefully through 100 American textbooks and standard references in the field of geology, to ascertain the listings given of foreign workers—not necessarily foreign publications. Comparisons were made with 100 British books and 50 each from Germany, France, Holland, and Switzerland. The results are shown in Table 1.

A glance through the respective journals of these countries illustrates a more serious provincial attitude on the part of American geologists. It is idle to harp about the Europeans' greater facility in languages and at the same time insist that all American science students be forced to learn some European language, at least for reading purposes.

During recent years, in visiting many universities in Europe and Asia, I have seen in various science departments wall charts, published in the United States, depicting such things as the divisions of the science of physics, highlights in the history of biological evolutionary thought, discoverers in the field of electromagnetism, and so on. In one chart showing discoverers in that particular science field, I noted that of 94 names listed, a mere 74 were Americans, and not a single Britisher was mentioned. It is bad enough that American students should be misinformed to this extent, but doubly serious when foreign students are handed this sort of propaganda. Although I do not wish to belittle the contribution of America toward science in general and geology in particular, is it not time to place such contribution in its true perspective, such as Marie Curie working in a cold, leaking, dingy laboratory on an infinitesimally small budget versus America with its air-cooled, centrally heated, luxuriously furnished laboratory struggling along on a \$10-million grant?

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21 February 1956

1 JUNE 1956

### Serum Protein Concentrations in the North American Negroid

Anthropological and medical differences between Negroids and Caucasoids have been the subject of much medical discussion (1). Studies on the chemical composition of blood have shown no consistent variation except in the concentrations of plasma proteins. Surveys in Africa (2), Jamaica (3), and the United States (4) report that Negroids have lower serum albumin and higher serum globulin values than Caucasoids residing in the same region. Male Caucasoids were found to have higher serum cholinesterase activities than a comparable group of North American Negroids (5). The increase in the globulins has been mainly in the gamma globulin fraction. These

differences have been attributed to infection with parasitic or tropical disease, liver disease, malnutrition, and possibly a genetic variance.

A blood-donor screening study for the detection of carriers of viral hepatitis in progress at the Hospital of the University of Pennsylvania provided an opportunity for comparison of Negroids and Caucasoids living in a nontropical area (6). Thirty-six percent of the Negroids and 63 percent of the Caucasoid donors were born, and had always lived, in the vicinity of Philadelphia. The donors, who ranged in age from 18 to 59 years, were accepted only if there was no history of jaundice, liver disease, syphilis, or serious systemic illness, and if the hemoglobin was greater than 12.5 g percent. Samples of blood were collected, and the following tests were performed (7): serological tests for syphilis, total and prompt direct (1') serum bilirubin, thymol turbidity and flocculation, cephalin-cholesterol flocculation, and zinc sulfate turbidity (6, 8).

The distribution of values for the zinc turbidity in Shank-Hoagland units of those donors who had normal results for all other tests are plotted in Fig. 1. The mean value for the Negroids is much higher than that of the Caucasoids ( $p < 0.001$ ). This difference is present irrespective of age or sex. Among the Caucasoids, the females have a significantly higher mean than the males.

In addition to the zinc turbidity test of Kunkel, which correlates with the concentration of the gamma globulin fraction (9), two other methods of measuring gamma globulin were used. Analysis of the serum of 31 Caucasoid and 25 Negroid donors by the ammonium sulfate turbidity test (10) gave values of  $2.50 \pm 0.16$  units for the Caucasoid and  $2.82 \pm 0.23$  units for the Negroid serums ( $p < 0.01$ ). Zone electrophoresis (11) of the serums of 45 Caucasoids showed a mean of  $18.04 \pm 4.41$  percent of gamma globulin and  $21.75 \pm 5.09$  percent for the 45 Negroids tested ( $p < 0.01$ ). The Negroids also had a lower mean concentration of serum albumin ( $p < 0.05$ ).

The finding of significantly higher mean concentrations of gamma globulin by these methods agrees with previous reports. However, the subjects in the present study were all voluntary donors who came from localities in which both racial groups were living in a similar environment in a region where there is no general malnutrition or endemic disease. No abnormalities in liver function were detectable by a series of tests. This suggests that the higher mean concentrations of gamma globulin found in Negroids may be the result of a genetic factor. The differences shown by the North American Negroid population are large enough to require the use of separate standard

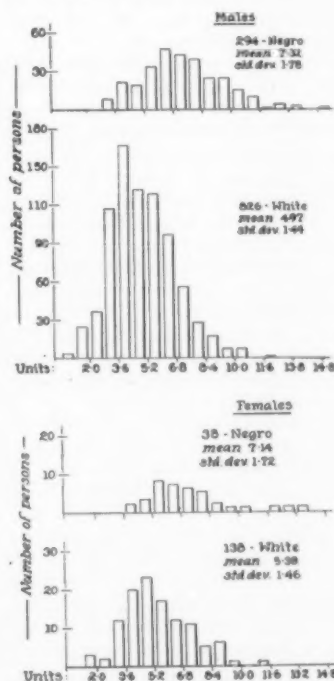


Fig. 1. Serum gamma globulin of Negroids and Caucasoids measured as zinc turbidity and expressed as Shank-Hoagland units.

values when gamma globulin and other serum protein measurements are made.

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14 December 1955

## Green Crabs and the Redistribution of Quahogs

In a recent report, Dow and Wallace commented on the effects of winter storms in redistributing populations of the quahog, *Venus mercenaria* L. (1). The probable effect of water currents in accumulating masses of young quahogs has been indicated elsewhere (2). Recently it has come to light that crabs also constitute a factor in the redistribution of a quahog population.

The green crab, *Carcinides maenas* (L.), is a voracious predator upon clam and quahog populations in northern New England waters (3, 4). Although other factors are also involved, its progressive increase in the Gulf of Maine has roughly paralleled a serious depletion of the soft-shelled clam, *Mya arenaria* L. (5), and the crab is an important factor in the reduction of seedbeds of the quahog (4). Data obtained during the fall of 1955 indicate that, in addition to its importance as a shellfish predator, the green crab plays a minor but appreciable role in redistributing quahogs in an area where crabs and quahogs occur together.

On 16 Sept. 1955, while repairing a fence impeding the entrance of crabs into Brickyard Cove, Sebascodegan Island, Me., we collected a green crab that was moving about with a 1-in. quahog pinched onto the tip of one of its walk-

ing legs. When the crab was lifted from the water, the quahog pinched down more tightly on the crab's leg, thus removing the tip of the terminal segment. The same action left a small circular nick, marking the two valves symmetrically, at the edge of the quahog shell. It was then noted that several quahogs lay exposed on screening that had been placed on the bottom behind the fence to reduce tidal erosion and on which the crab with the attached quahog had been collected. Of a sample of 32 of these exposed quahogs, 26 were living, and in 24 of these the edges of the valves were scarred by nicks similar to that described. In the other two living specimens, growth had continued after scarring so that each valve was marked near the edge by a semicircular scar, and its concavity was filled in by new growth.

It is assumed that the quahogs found on the flat screening had been transported there by the movements of crabs and that once over the screening the quahogs had either been shaken off or had amputated the tips of the crab legs, thus freeing themselves. It is further assumed that a quahog becomes attached to a crab's leg when a crab inadvertently places a leg tip between the open valves of a quahog in the region of the pallial sinus as the latter rests upright in the mud.

These assumptions are strengthened by the following observations. Small quahogs are frequently collected about the periphery of Quahog Bay, of which Brickyard Cove is an arm, each with a small circular nick in the edge of the shell in the region of the pallial sinus. When a quahog is opened immediately after it has pinched off the tip of a crab leg, it is found that the tip lies between the valves near a circular nick at the edge of the shell. Green crabs with missing leg tips occur frequently in the area. Robert L. Dow and Dana E. Wallace of the Maine Department of Sea and Shore Fisheries have observed a horseshoe crab, *Limulus polyphemus* L., at the moment that it picked up a quahog passenger in the manner postulated for the green crab; they have photographed the specimens involved.

After the observations of 16 Sept., we collected a random sample of 1000 quahogs, all under 5 cm and more than 1.5 cm, in Brickyard Cove. Of these specimens, 29, or 2.9 percent, demonstrated a circular nick at the edge of the shell, or a shell bilaterally marked by semicircular scars that had been filled in by subsequent growth. Of the specimens thus far examined, the smallest in which the nick, either peripheral or elsewhere, has been detected has been 2 cm in length; the largest, 3.7 cm.

The role of the green crab in redistributing the quahog may not be especially

important to the whole ecology of either, but it may be that something of a beneficial effect is introduced by the green crab in thinning crowded populations, since it would be in such areas that the walking legs would seem most likely to enter the valves. On the other hand, the breaks introduced may allow entrance to foreign invaders or to the action of green crab pincers, thus increasing the susceptibility of the quahog to destruction. However, a sample of several empty scarred valves that were collected showed that the nick was in a peripheral position in but one case.

One value of the observations reported here may lie in a possible correlation between frequency of the scar reported and the relative populations of green crabs and quahogs. On the other hand, the frequency of missing leg tips of the green crab in a quahog area might reasonably be presumed to be related to the density of small quahogs in the feeding zone.

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22 December 1955

## Serotonin-Releasing Activity Limited to Rauwolfia Alkaloids with Tranquilizing Action

Previous findings (1, 2) have led us to postulate that the clinical effects of reserpine are mediated through serotonin (5-hydroxytryptamine), a substance that is normally present in the brain, and that serotonin may have a role in brain function. This concept is based in part on the observation that reserpine liberates serotonin from its body depots. The evidence presented in this paper strengthens the concept by showing that of a number of centrally acting drugs only *Rauwolfia* alkaloids exerting a tranquilizing action effect the liberation of brain serotonin.

Rabbits received the various drugs intravenously and were killed 4 hours later. Their brains were removed as rapidly as possible, and serotonin was determined fluorometrically (3).

In Table 1 is shown the effect of a

Table 1. Serotonin concentration in rabbit brain 4 hours after administration of various *Rauwolfia* alkaloids. Rabbits received 2 mg/kg of alkaloid intravenously (25 mg of each compound was dissolved in a few drops of glacial acetic acid and diluted with 0.7 ml ethanol, 0.7 ml propylene glycol, and 3.6 ml water.)

Alkaloid	No. of animals	Sedative action	Serotonin content (µg/g)
None	9		0.57 ± 0.08
Reserpine	2	Active	0.05, 0.07
Deserpidine (recalescine)	2	Active	0.06, 0.13
Rescinnamine	2	Active	0.09, 0.12
Isoreserpine	2	Inactive	0.42, 0.54
Methyl reserpate	2	Inactive	0.43, 0.45
Reserpilic acid	2	Inactive	0.48, 0.55
Reserpinine	1	Inactive	0.49
Serpentine	2	Inactive	0.43, 0.46
Ajmaline	1	Inactive	0.44
Ajmalacine	2	Inactive	0.52, 0.58
p-Toluene sulfonyl methyl reserpate	1	Inactive	0.49
Yohimbine	1	Inactive	0.48

Table 2. Serotonin concentration in rabbit brain 4 hours after intravenous administration of various drugs that act on the central nervous system.

Drug	Dose (mg/kg)	Central effect	Serotonin content (µg/g)
None			0.57 (avg.)
Phenobarbital	100	Hypnosis	0.51
Barbital	200 (divided doses)	Hypnosis	0.51, 0.48
Morphine	20	Sedation	0.43, 0.57
Scopolamine	50	Light sedation	0.50
D-Amphetamine	70 (divided doses)	Convulsions	0.55
Diphenhydramine	35 (divided doses)	Convulsions	0.54
Cortisone	26 (divided doses)	Convulsions	0.49

Table 3. Serotonin concentration in rabbit brain 4 hours after intravenous administration of various hallucinogenic and psychotherapeutic drugs.

Drug	Dose (mg/kg)	Central effect	Serotonin content (µg/g)
None			0.57 (avg.)
LSD	0.12	Excitement	0.47, 0.49
Mescaline	75	Excitement	0.46, 0.50
Chlorpromazine	10	Sedation	0.52, 0.49
Frenquel	75 (divided doses)	Convulsions	0.53, 0.59

number of *Rauwolfia* alkaloids on brain serotonin. Only reserpine, rescinnamine, and deserpidine (recalescine) induced sedation and caused a significant alteration in brain-serotonin levels. Methyl reserpate, an inactive hydrolytic product of reserpine, did not release serotonin. Other alkaloids that are structurally related to reserpine had neither a sedating action nor an effect on brain serotonin. The failure of isoreserpine to release serotonin or to produce an ob-

servable sedative effect was of particular interest, since this compound differs from reserpine only in steric configuration (4).

Table 2 shows the effect on brain serotonin of other centrally acting drugs that are structurally unrelated to reserpine. It can be seen that a variety of hypnotics, narcotic analgesics, and central nervous system stimulants had no effect on brain serotonin.

The effect of a number of hallucinogenic agents and synthetic psychothera-

peutic drugs is shown in Table 3. None of the compounds studied changed significantly the serotonin content of brain tissue. Since previous studies have shown that the hallucinogenic agent, lysergic acid diethylamide (LSD), antagonizes a central action of reserpine (1), it seemed possible that pretreatment with LSD would prevent the release of serotonin by reserpine. It was found, however, that LSD did not block this release, which indicates that LSD inhibits reserpine centrally by blocking the action of liberated serotonin, as previously suggested (5).

Of special interest was the inability of chlorpromazine to release serotonin, since, like reserpine, chlorpromazine exerts tranquilizing effects, potentiates hypnotics, and is useful in the treatment of psychiatric disorders. Presumably, therefore, the central actions of chlorpromazine are not mediated through the release of serotonin. This is in accord with our observation that LSD blocks the reserpine-induced potentiation of hypnotics but not that induced by chlorpromazine (6). It thus seems likely that chlorpromazine acts directly on receptor sites in the brain. This is in contrast to reserpine, which acts through serotonin. Frenquel, a new drug that is currently under investigation for the treatment of psychiatric disorders, also failed to release serotonin in brain tissue.

The experiments described here show that, of a wide variety of drugs that act on the central nervous system, only the *Rauwolfia* alkaloids that cause sedation can affect brain serotonin. They offer further evidence that the beneficial clinical effects of these drugs are mediated through the action of serotonin.

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- \* Guest worker from Hoffmann-La Roche, Inc., Basel, Switzerland.

2 December 1955

Chemistry has been termed by the physicist the messy part of physics, but that is no reason why the physicists should be permitted to make a mess of chemistry when they invade it.—FREDERICK SODDY.

## Book Reviews

**Reflections of a Physicist.** P. W. Bridgman. Philosophical Library, New York, ed. 2, 1955. xiv + 576 pp. \$6.

This book is a collection of talks delivered or papers presented on various occasions on topics concerning mainly the idea of operationalism as advocated by the author as *the* method of science, the so-called epistemological bearings of modern physics (especially relativity theory and quantum theory), and views on the social situation of our time. Being a European scientist and philosopher, I will be allowed, it is hoped, to say that P. W. Bridgman's opinions are not well enough known on the Continent, which is regrettable, because they are interesting and very original. But one may doubt whether it would be correct to consider them as falling into the classical realm of philosophy. The number of scientists who engage on a philosopher's pilgrimage increases—not always very happily, for in many cases a serious study of philosophy prior to the pilgrimage would have avoided both a naive position and an awkward use of philosophic concepts. Yet Bridgman has escaped the danger by developing some genuine ideas and a simplicity of exposition that reminds one a little of Hume. He is very Anglo-Saxon in the presentation of his argument which reflects the conclusions from his own experience.

Since the book is a second edition (containing some additions to the first one), its contents may be known to former readers. The scientist and philosopher will not find anything really new in it.

The main ideas of Bridgman's thought should be recalled: (i) the operational aspect; (ii) the private aspect of all scientific activity (prior to its public aspect). Science is an *activity*. Science has been contaminated by an overemphasis of the social factor. Science is, nevertheless, objective (this point is very well presented). In the analysis of the private and public level, he reminds us that the discovery of the private level (p. 75) "is almost always the result of some bitter experience"—this I can agree with.

These ideas and many more are pre-

sented in the first nine sections, which are a series of expositions all saying more or less the same thing. Of the following sections 10 to 17, which serve as illustrations, the same must be said. Some of the contributions date back quite a few years, and one gets the feeling on reading them that not all these things are new anymore. But they are always very well said, and the nonscientist in particular will profit by the lecture.

Whoever is not familiar with Bridgman's thesis on operationalism would do well to begin by reading section 6, for he could easily get lost by beginning with section 1. One of the best illustrations I find is given in section 13, which is an excellent discussion of the second law of thermodynamics from the operational point of view. In other sections, the writing is sometimes too long for what is really involved. The fact that the book is a collection of essays presented elsewhere has the inevitable consequence of repetitions, of which there are a good many.

In reading this book I was struck by one point that I never had realized before, namely, that the philosophic genre described as solipsism is really possible. Bridgman seems to me to be a genuine representative of that way of thought, and I respect him all the more, for his argument makes very good sense and is never offered for the sake of argument alone, as so often happens in conventional philosophic dispute. Yet a position like this is a rare thing, and I doubt whether it will have any future.

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**Physiologie der Zelle.** Johannes Haas. Gebrüder Borntraeger, Berlin, 1955. 474 pp. Illus. DM 48.

"The elementary constituent of all living substances and the substratum of all elementary vital processes is the cell. Hence, if the task of physiology lies in the explanation of the vital phenomena, it is evident that general physiology can

be only cell physiology." With these words, Verworn introduced his *General Physiology* in 1894.

Now physiology deals with the dynamics of structure and ultimately with changes on a molecular level that are associated with the various activities of living matter. The discoveries of the cell morphologists at the end of the 19th century were indeed breath-taking, and they deeply influenced the thinking in all branches of biology. But they did not provide the basis for a true cell physiology as Verworn had hoped because their structures were still too far removed from the molecular level and thus for decades cytology and physiology went their separate ways. Cytology remained largely static while general physiology resorted to physical-chemical models and guesswork. There was no real physiology of the cell because we had no morphology of the cell in terms useful to the physiologist.

In recent years, developments in many different fields of biology have laid the foundations for such a physiology of the cell. The book by Haas is an attempt to collect the scattered results from modern chemistry, enzymology, cytochemistry, electron microscopy, genetics, embryology, and so forth, and to fit them into a physiology of the cell. The task is tremendous. It asks for a synthesis of classical cytology, modern quantitative cytology, cell chemistry, submicroscopic morphology, chemistry of macromolecules, and biochemistry.

It is obviously impossible for a single individual to know and evaluate critically the vast literature in all these areas, and the book is therefore largely based on existing reviews in these fields. In general, the author has succeeded in giving an interesting and balanced picture of the problems, methodology, and achievements of modern cell biology and in conveying some of the feeling of excitement that is associated with the vigorous expansion into new areas of exploration and the synthesis of previously unconnected branches of knowledge.

The organization of the book indicates the scope of modern cell physiology. (i) General properties of macromolecules; colloid chemistry of macromolecules; structure and properties of proteins and nucleic acids; general properties of enzymes and their distribution in the cell; and chemistry and molecular structure of lipids. (ii) Organization of the cell: ground substance of the cytoplasm; cell surface; mitochondria and microsomes; and the nucleus and its morphology, chemistry, enzymology, and functions. (iii) Interphase chromosomes; physiology of gene action; and gene duplication and mutation. (iv) Functions of the cell: glycolysis, respiration, energy transfers, and kinetics of membranes. (v) Cell

division, cell growth, differentiation of cells, and embryonic induction.

It seems unavoidable that in covering such a variety of rapidly expanding disciplines, the treatment should be uneven and often out of date. The coverage of the literature is often spotty, especially since 1950. The recent work on cell structure with the electron microscope is largely neglected and, as a result, the discussion of the "ground substance" of the cytoplasm is especially weak and based mainly on the speculations in the German literature before 1950. Sometimes different chapters come to contradictory conclusions: chromosome reproduction occurs in prophase on one page, but all the evidence for synthesis during interphase is presented in a later chapter. The expert in each of the fields covered will no doubt be annoyed by such discrepancies, by the omission of significant work, by the emphasis in some chapters on ancient speculations, and perhaps by the frequent misspelling of names. It is hoped that in a future edition the various chapters will be revised by experts in the respective areas.

Yet, despite these shortcomings, the book is a rich source of information, and it is unique in scope and conception. It deserves the attention of anyone who is interested in the activities of cells and the modern approaches to their investigation.

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**Ergebnisse der Medizinischen Grundlagenforschung.** K. Fr. Bauer. Thieme, Stuttgart, Germany, 1956 (order from Intercontinental Medical Book Corp., New York 16). 855 pp. Illus. \$30.75.

As the title indicates, this book is largely concerned with giving an account of the present state of the basic sciences that underlie medicine. The several chapters are "Structure of bacterial surfaces," by J. Tomcsik; "The present state of fundamental research in the field of tuberculosis from a dermatological viewpoint," by C. F. Funk; "The mitochondria," by G. Glimstedt and S. Lagerstedt; "The fine structure of nucleus and cytoplasm in relation to general cell functions," by F. E. Lehman; "Metabolites and antimetabolites," by J. C. Somogyi; "Kinetic and thermodynamic enzyme reactions in living cells and tissues," by H. Holzer; "Results of vitamin research from 1950 to 1954," by W. Stepp; "Fundamental processes of muscular contraction," by A. Fleckenstein; "The essential amino acids," by J. Kapfhammer, R. Bauer, and V. Kapfhammer; "Tissue and functional therapy,"

by S. Funaoka; "The mechanism of parenteral tissue and stimulus therapy," by K. O. Vorlaender; "The present state of research in allergies," by F. Sheiffarth; "Biophysics of radiation," by F. Wachsmann; "Hypothermy," by H. Laborit; "Recent results in neurohistology," by E. Landau; "The development of the human cerebral cortex," by G. von Bonin; "The external and internal functional relationship of the hypophyseal organs," by E. Collin; and "Embryology in relation to medical research," by G. Töndury.

There are both author and subject indexes.

**International Review of Cytology.** vol. IV. G. H. Bourne and J. F. Danielli, Eds. Academic Press, New York, 1955. xii + 419 pp. Illus. \$9.

The fourth volume of these reviews includes 12 articles assembled in accordance with the stated policy of the editors to survey the expanding field of cellular biology over a period of years. Selected topics range from a consideration of nucleic acids as ubiquitous cell components to examination of the properties of highly specialized cell types.

"The histochemistry of nucleic acids" is reviewed by N. B. Kurnick in a comprehensive manner. Emphasis is placed on the rigid requirements essential to critical analysis of these materials *in situ* by photometric, enzymatic, and staining procedures. Some of the same problems are examined by R. Vendrely in the "Histochemistry of bacteria," although constituents of bacterial cells other than nucleic acids are also considered. The short chapter by A. Marshak on "Bacterial cytology" sounds the precautionary note that students of the nuclear apparatus should rely on direct analysis and avoid the tendency "to seek in bacteria the morphological counterparts of intracellular structures seen in higher forms."

L. E. Wagge discusses in considerable detail the structure and function of "Amoebocytes," primarily as they occur in the Mollusca, but with reference to wandering cells in other phyla. This review, and the parallel study of Harald Moe on the mucus-secreting "goblet cells, especially of the intestine of some mammalian species," afford insight into the origin and structural modifications of cells concerned with transport and secretion.

Another outstanding review is D. P. Hackett's "Recent studies on plant mitochondria," in which morphological, biochemical, and physiological studies are evaluated, but which is devoid of illustrative material that could have en-

hanced its usefulness. R. Mühlethaler's consideration of the "Structure of chloroplasts" includes many of the more recent findings with respect to the ultra-fine structure afforded by electron microscopy. M. Wolman surveys "Problems of fixation in cytology, histology, and histochemistry," presenting a treatment of general principles and problems in which the choice of a fixing agent to meet individual requirements is stressed, although specific formulas are not provided.

A review by W. S. Vincent of the "Structure and chemistry of nucleoli" includes results that he obtained in the study of nucleoli isolated from starfish oocytes; this article emphasizes the uncertain state of current knowledge despite the considerable progress that has been made in recent years toward an understanding of nucleolar structure and function. Localization of "Cholinesterases at neuromuscular junctions" is discussed by R. Couteaux and illustrated with photographs and diagrams. E. J. Conway contributes the second part of a discussion that was initiated in volume II of this series entitled "Evidence for a redox pump in the active transport of cations." The introductory chapter by M. J. Kopec on "Cytochemical micrurgy" lists some of the technical developments that facilitate quantitative study of small parts of cells.

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**Yearbook of Anthropology, 1955.** vol. I. William L. Thomas, Jr., Ed. Wenner-Gren Foundation for Anthropological Research, New York, 1955. xv + 836 pp.

The increasing importance of anthropology and the growing volume of its literature were appropriately marked in 1953 by the publication of an encyclopedic appraisal, *Anthropology Today* (edited by A. L. Kroeber *et al.*). The present *Yearbook of Anthropology*, benefiting from the experience of its predecessor, inaugurates a new series of annual publications and marks anthropology's full coming of age.

Although it focuses on the significant achievements and trends in the field of anthropology during 1952-54, the first volume of the *Yearbook* is truly a synthesis of heroic proportions. Excluding the editor and his staff, more than 40 contributors are involved; these include, to mention only a few, Birket-Smith, Eiseley, Firth, Hauri, Koppers, Kroeber, Schultz, and Tax.

This book is divided into six sections. Part one is devoted to a "Guest editorial" by Julian Huxley on evolution.

Part two ("Man's past: environments, relics, ancestors") addresses itself to the anthropological problems, methods, and theories that emphasize time-depth. Part three ("Other considerations of theory") touches on supplementary questions of method and theory, with the primary emphasis on process rather than time. Part four ("Practical affairs") discusses the practical achievements of anthropology and its influences both on the general public and in the fields of education, art, industry, and government. Part five ("Regional round-up: Europe and southwest Asia"), the first of an annual series of areal round-ups, contains reports on anthropological activities in various countries as seen by scholars who are active in the countries or regions under discussion. Part six is devoted to "Reference data" and includes a listing of medals, awards, and memorial lectures in anthropology; of professional associations; and of doctoral dissertations in anthropology submitted to the various universities of the world. The admitted gaps in reference information will be filled in future issues, but the magnitude of the task is indicated by the fact that the lists go back to the turn of the century and run through the end of 1954.

It is difficult to do justice to such an important (and handsome) book in a brief review. It is not a collection of abstracts, although these may appear in future issues; and it is possible that certain papers are too wide in scope. However, the *Yearbook's* format is fluid and, quite apart from the cyclical nature of the regional round-ups, different contributors and new developments will lend a special flavor to each succeeding volume.

This book is addressed to anthropological specialists, to scholars and students in other disciplines, and to the educated public. It is a measure of the *Yearbook's* worth that it can be read with pleasure and profit by such a diversified group. However, it must be noted with regret that this book, being frankly experimental, was not intended for commercial sale. Text and trade editions, comprising parts one through three, will be published this year by the University of Chicago Press.

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## Books Reviewed in

### The Scientific Monthly, June

*Niels Bohr and the Development of Physics*, W. Pauli, Ed., assisted by L. Rosenfeld and V. Weisskopf (McGraw-Hill; Pergamon). Reviewed by B. T. Feld.

*The Microbes' Contribution to Biology*, A. J. Kluyver and C. B. Van Niel (Harvard University Press). Reviewed by M. H. Adams.

*The Caves Beyond*, J. Lawrence, Jr., and R. W. Brucker (Funk & Wagnalls). Reviewed by A. C. McFarlan.

*Biochemistry: an Introductory Textbook*, F. Haurowitz (Wiley; Chapman & Hall). Reviewed by M. Korzenovsky.

*Molecular Beams*, K. F. Smith (ed. 2 of *Molecular Beams*, by R. Fraser), (Methuen; Wiley). Reviewed by I. Estermann.

*Science and Freedom, a Symposium*, Congress for Cultural Freedom (Beacon). Reviewed by N. Rashevsky.

*The Secret of the Hittites*, C. W. Ceram (American ed. 1, Knopf). Reviewed by G. W. Van Beek.

*The Unleashing of Evolutionary Thought*, O. Riddle (Vantage). Reviewed by P. B. Sears.

*The Expression of the Emotions in Man and Animals*, C. Darwin (authorized ed., Philosophical Library). Reviewed by A. Reissner.

*Observational Astronomy for Amateurs*, J. B. Sidgwick (Faber and Faber, distributed by Macmillan). Reviewed by J. Q. Stewart.

*Wild America*, R. T. Peterson and J. Fisher (Houghton Mifflin). Reviewed by A. E. Eynon.

## New Books

*Weather Analysis and Forecasting*, vol. 1. *Motion and Motion Systems*. Sverre Pettersen. McGraw-Hill, New York, ed. 2, 1956. 428 pp. \$8.50.

*Earth, Sky and Sea*. Auguste Piccard. Translated by Christina Stead. Oxford University Press, New York, 1956. 192 pp. \$4.

*Principles of Embryology*. C. H. Waddington. Macmillan, New York, 1956. 510 pp. \$7.50.

*Agricultural Ecology*. Girolama Azzi. Constable, London, 1956 (order from Essential Books, Fair Lawn, N.J.). 424 pp. \$7.20.

*What Makes a College? A History of Bryn Mawr*. Cornelia Meigs. Macmillan, New York, 1956. 277 pp. \$5.

*Perception and the Representative Design of Psychological Experiments*. Egon Brunswik. University of California Press, Berkeley, 1956. 154 pp. \$5.

*Biology*. Relis B. Brown. Heath, Boston, 1956. 658 pp. \$6.50.

*The Biochemistry and Physiology of Bone*. Geoffrey H. Bourne, Ed. Academic Press, New York, 1956. 875 pp.

*The Direction of Human Development*. Biological and social bases. M. F. Ashley Montagu. Harper, New York, 1955. 404 pp. \$5.

*Plane Trigonometry*. E. Richard Heinemann. McGraw-Hill, New York, ed. 2, 1956. 239 pp. \$3.75.

*New Concepts of Healing*. Medical, psychological, and religious. A. Graham Ikin. Association Press, New York, 1956 (rev. American edition; printed in Great Britain by Hodder & Stoughton, 1955). 262 pp. \$3.50.

*Modern Naval Architecture*. W. Muckle. Philosophical Library, New York, 1956. 154 pp. \$4.75.

*Modern Marine Engineering*. D. W. Rudorff. Philosophical Library, New York, 1956. 154 pp. \$4.75.

## Miscellaneous Publications

(Inquiries concerning these publications should be addressed, not to Science, but to the publisher or agency sponsoring the publication.)

*Taxonomic Appraisal and Occurrence of Fleas at the Hastings Reservation in Central California*. Publ. in Zoology, vol. 54, No. 5. Jean M. Linsdale and Betty S. Davis. 78 pp. \$1.50. *The Frankliniella Occidentalis (Pergande) Complex in California (Acarina: Trombiculidae)*. Publ. in Entomology, vol. 10, No. 6. Douglas E. Bryan and Ray F. Smith. 52 pp. \$0.75. *The Larval Trombiculid Mites of California (Acarina: Trombiculidae)*. Publ. in Entomology, vol. 11, No. 1. Douglas J. Gould. 116 pp. \$2. University of California Press, Berkeley-Los Angeles, 1956.

*International Scientific Radio Union, Proceedings of the XIth General Assembly*. Held in The Hague from 23 August to 2 September 1954. vol. X, pt. 7, *Commission VII on Radioelectronics*. International Scientific Radio Union, Brussels, Belgium, 1954. 140 pp. \$3.

*American Malacological Union and American Malacological Union Pacific Division, Annual Reports for 1955*. With membership list revised 31 December 1955. Bull. 22. Buffalo Museum of Science, Buffalo, N.Y., 1956. 58 pp.

*Copper Wire Tables*. NBS Circular 31. U.S. National Bureau of Standards, Washington 25, ed. 4, 1956 (order from Supt. of Documents, GPO, Washington 25). 36 pp. \$0.30.

*Laboratory Tests in Common Use*. Solomon Garb. Springer, New York, 1956. 160 pp. \$2.

*Fine Structure of Cells*. Symposium held at the VIIth Congress of Cell Biology, Leiden, Belgium, 1954. International Union of Biological Sciences, Ser. B, No. 21. Noordhoff, Groningen, Netherlands, 1955. 321 pp.

*Secondary Elasticity*. A general mathematical theory of elastic secondary stress in continuous media. Monogr. Ser. No. 1, vol. 1, No. 1. P. L. Sheng. Chinese Association for the Advancement of Science, Taiwan, 1955. 138 pp.

*International Technical Conference on the Conservation of the Living Resources of the Sea, Papers Presented*. Rome, 18 April-10 May 1955. United Nations, New York, 1956 (order from Columbia University Press, New York). 371 pp. \$3.

*Statistical Analysis of Highway Accidents*. Highway Research Bd. Bull. 117. 31 pp. \$0.75. *Effects of Chlorination and Microorganisms and Constituents of Asphalts*. Bull. 118. 48 pp. \$0.90. *Factors Influencing Travel Patterns*. Bull. 119. 94 pp. \$1.80. *The Use of Chemical Additives in Food Processing*. A report by the Food Protection Committee of the Food and Nutrition Board. Publ. 398. 91 pp. \$2. National Academy of Sciences-National Research Council, Washington, 1956.

*L'Alimentation minérale du bétail au Congo Belge*. Série Technique No. 48. L. Hennaux. Institut National pour l'Étude Agronomique du Congo Belge, Brussels, Belgium, 1956. 115 pp. F. 160.

*Marine Polychaete Worms from Laborador*. Proceedings, vol. 105, No. 3361. Marian H. Pettibone. U.S. National Museum, Washington, 1956. 54 pp.

## Scientific Meetings

### Cosmic-Ray Colloquium

The Midwest Cosmic-Ray Colloquium has been meeting now at various midwestern universities for about 5 years. Usually, one or two meetings are held each year. The interest has grown so much that the recent meeting at the University of Minnesota was extended into a 2-day meeting, with the first day occupied by discussions of primary cosmic rays and the second day by discussion of high-energy particle physics.

Papers on the first morning program were concerned with general measurements of the primary radiation and recent results on the soft radiation above the atmosphere, by the Universities of Iowa and Minnesota. The afternoon session was concerned with a discussion of the large solar eruption of 23 Feb. 1956, during which the largest increases in cosmic-ray intensity so far observed were recorded. In this respect the meeting was timely, because many of the important data were at hand from both high-altitude flights and sea-level monitoring stations. It is known that the sun at this time emitted a large amount of cosmic radiation extending up to  $20 \times 10^9$  volts, which increased normal cosmic-ray intensities by at least a factor of 20 and probably more at the top of the atmosphere. The cosmic rays died away exponentially with time, and the effects of the flare had disappeared in 24 hours. Results were presented by Iowa, Chicago, and Minnesota.

Sessions on the second day were concerned with reports of emulsion and cloud-chamber work on the heavy mesons and hyperons by groups from Chicago, Wisconsin, Indiana, Minnesota, Purdue, and Nebraska. The program proceeded at a fairly leisurely pace with ample time for discussion. There seems to be a solid interest among the midwestern universities in this work, and bids have already been made for entertaining the colloquium at later dates.

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### Meeting Notes

■ More than 500 specialists in sound and noise control will participate in the second International Congress on Acoustics

that will take place in Cambridge, Mass., 17–23 June, under the sponsorship of the International Commission on Acoustics. Harvard University and the Massachusetts Institute of Technology will be joint hosts for the meeting, which will be held in conjunction with the 51st meeting of the Acoustical Society of America.

More than 100 technical contributions have been received from abroad: they will be presented by scientists from Argentina, Belgium, Canada, Denmark, England, France, Germany, Hungary, India, Italy, Japan, the Netherlands, Norway, the Soviet Union, the Saar, Sweden, and Turkey. The technical program will be organized around three major symposia: (i) bioacoustics and noise control—human responses to sound (including hearing, psychological response, and biological effects) and noise-control methods to meet these responses; (ii) architectural and musical acoustics—the production of music and speech sounds and the design of enclosures for good hearing conditions; and (iii) physical acoustics and sonics—acoustical studies of matter, propagation of sound, and application of acoustical techniques to technical problems.

There will be special demonstrations of speech analysis and syntheses, and exhibits will be prepared for the congress by many scientific, technical, and manufacturing concerns throughout the world. Richard H. Bolt, director of the Acoustics Laboratory at the Massachusetts Institute of Technology, is chairman of the planning committee for the congress, and John A. Kessler, administrative officer in the Acoustics Laboratory, is congress secretary.

■ The new Arizona Academy of Science is now well established. Some 125 people participated in the first organizational meeting, at which a provisional constitution was approved and the following officers were elected: pres., Alan T. Wager, Arizona State College; pres.-elect, Albert R. Mead, University of Arizona; sec., Albert G. Wilson, Lowell Observatory, Flagstaff; treas., Virgil E. Bottom, Motorola Research Laboratory, Phoenix.

At a second meeting chairmen were appointed for standing committees and the petitions of sections desiring organization were received. The industrial research section already is active and has

more than 50 members. At this meeting charter membership was extended to 30 Apr. 1956 so that there are approximately 300 charter members. In addition, tentative plans were made for both a fall meeting and a spring meeting, the latter to be held in conjunction with the Southwestern and Rocky Mountain Division meeting of AAAS that is scheduled to take place 28 Apr.–2 May 1957 at the University of Arizona.

The academy owes its existence, in part, to the encouragement of C. M. Goethe, who had deposited funds with the treasurer of AAAS to be used to help defray the expenses of the organization of an academy of science in Arizona. When he learned of the plans for such a group, he made further contributions directly to the organizers. Fifty dollars of such funds were designated by him to assist in the formation of a junior academy. Since the organizing meetings were held, Goethe has again contributed.

■ A 2-day symposium, New Horizons in Astronomy, will be held in celebration of the dedication of the University of Pennsylvania's new Flower and Cook Observatory, near Paoli, Pa., 11–12 June. Astronomers from Europe and the United States will present papers. Otto Struve, director of the Leuschner Observatory (University of California), will preside.

The first day will be devoted largely to reports on developments in electronic observation; the second day, to astronomy itself. Underlying the whole symposium will be an emphasis on the future of telescopes of moderate size.

The actual dedication, which will take place on the first evening, will be highlighted by the first formal demonstration of the Newton Lacy Pierce memorial photometer, development of which was started by Pierce of Princeton University before his death in 1950. The Pierce photometer embodies advanced practices in electronic observation. It measures star brightness by the pulse-counting technique (counting the groups of electrons given off by a photocell struck by starlight), thereby feeding digital data into an automatic printer. Moreover, it observes two stars simultaneously, using one of known brightness as a reference in gauging the intensity of the other.

To close the symposium, Fred Whipple, director of the Smithsonian Institution's Astrophysical Observatory, will report on "The artificial satellite—the first man-made astronomical object."

Participants from abroad include André Lallemand, Laboratoire de Physique Astronomique, Observatoire de Paris, France; "La télescope électronique"; J. D. McGee, Imperial College of Science and Technology, University of London, England; "The charge image integrating tube"; and Peter Fellgett,

Cambridge University, England, "Television techniques in modern astronomy."

The new Flower and Cook Observatory combines the functions of Pennsylvania's old Flower Observatory, Highland Park, Pa., and Cook Observatory, Wynnewood, Pa., retaining the names of the late donors, Reese Wall Flower and Gustavus Wynne Cook. The L-shaped building is surmounted at one end by a 27-foot movable dome. It houses a 28½-inch reflecting telescope and a 15-inch horizontal telescope with a siderostat.

■ The 88th annual meeting of the Kansas Academy of Science was held at Southwestern College 26-28 Apr. The Kansas Psychological Association also participated in the program. Approximately 100 papers representing the fields of botany and microbiology, chemistry, geology, physics, psychology, and zoology were presented. In addition, the best 21 papers given at the district meetings of the junior academy were integrated into the senior academy program. D. J. Ameel, head of the department of Zoology at Kansas State College, and president of the academy, delivered the principal address, "Maintenance of parasitism."

■ At least 1500 members of the American Society for Engineering Education, which includes engineering teachers from more than 150 American colleges and universities, are expected to attend the society's 64th annual meeting 25-29 June at Iowa State College. More than 200 papers devoted to increasing the effectiveness of American engineering education will be given during the 5-day period.

In addition to reports on current projects of the society, the principal interests at the meeting will focus on such topics as the impact of recent research on engineering education, the college faculty crisis, engineering training for the nuclear industry, and future trends in the supply and demand for engineering graduates.

Maynard M. Boring, president of the society, will deliver his presidential address at the convention's second general session on 26 June. He is consultant on engineering manpower for the General Electric Company and has been for many years active in the Engineering Manpower Commission of the Engineers Joint Council.

Sen. Bourke B. Hickenlooper (R., Ia.), formerly chairman and now member of the Joint Committee on Atomic Energy, is to be the principal speaker at the annual banquet. He will discuss "Some peaceful uses of atomic energy."

Others scheduled to give major papers during the week-long convention include Earl P. Stevenson, chairman of the board of Arthur D. Little, Inc.; James H. Hil-

ton, president of Iowa State College; Merrill M. Flood of the Columbia Research Foundation; W. G. Van Note, president of Clarkson College of Technology; and William L. Everitt, dean of engineering at the University of Illinois.

■ "High temperature—a tool for the future" is the theme chosen for a symposium that is to be held at the University of California, Berkeley, 25-27 June. The university and the Stanford Research Institute are cosponsoring the meeting, which is expected to attract 350 metallurgists, ceramists, geologists, physicists, chemists, and engineers. The discussions will deal with advances in the major fields of high-temperature research. The keynote speaker at the luncheon on 26 June will be Theodore von Karman, chairman of the Advisory Group for Aeronautical Research and Development, a NATO agency with headquarters in Paris, France.

The opening day panels will be devoted to "Methods of reaching high temperatures" and will have as cosponsor the Air Office of Scientific Research, U.S. Air Research and Development Command. Chairman will be Nevin K. Hiester, manager of S.R.I.'s chemical engineering section; assistant chairman will be Joseph A. Pask, professor of ceramic engineering at the University of California. Speakers will discuss solar, arc, and flame images, electric heat, and chemical and nuclear processes as sources of temperatures as high as 18,000°F.

The National Science Foundation will cosponsor the second day's program on "Materials for containing high temperatures." Alan W. Searcy, U.C. associate professor of ceramic engineering, will chair the proceedings, aided by Thomas E. Tietz, S.R.I. associate physical metallurgist, as assistant chairman. This session will deal with structures and properties of materials for high-temperature use and equilibrium and kinetic considerations involved in their environmental interactions.

The symposium will close with a discussion of "Processes occurring at high temperatures." The Office of Naval Research will be cosponsor for the day. Leo Brewer, U.C. professor of chemistry, and Marjorie W. Evans, S.R.I. senior physical chemist, are to be chairman and assistant chairman, respectively. This gathering will discuss such chemical responses under high temperatures as gas-state and condensed-state reactions and gas- and condensed-phase interactions.

### Society Elections

■ American Academy of Arts and Sciences: pres., John E. Burchard, Massachusetts Institute of Technology; v. pres. for mathematical and physical sciences,

John H. Van Vleck, Harvard University; v. pres. for biological sciences, Hudson Hoagland, Worcester Foundation for Experimental Biology; v. pres. for social arts and sciences, David F. Edwards, Saco-Lowell Shops, Boston; v. pres. for the humanities, W. Freeman Twaddell, Brown University; sec., Bruce H. Billings, Baird Associates, Cambridge, Mass.; treas., Thomas B. Adams, Sheraton Corporation, Boston.

■ American Association of Anatomists: pres., E. A. Boyden; pres. elect, Barry J. Anson; pres. emeritus, Samuel R. Detwiler; 1st v. pres., William W. Greulich; 2nd v. pres., O. V. Batson; program sec., Oliver P. Jones; sec.-treas., Louis B. Flexner.

■ American Association of Physical Anthropologists: pres., Mildred Trotter, Washington University School of Medicine; v. pres., Joseph B. Birdsall, University of California; sec.-treas., James N. Spuhler, University of Michigan. Representatives to the AAAS Council are J. Lawrence Angel and Carleton S. Coon.

■ Iowa Academy of Science: pres., W. F. Loehwing, State University of Iowa; v. pres., J. J. L. Hinrichsen, Iowa State College; sec.-treas. and representative to the AAAS Council, Jean L. Laffoon.

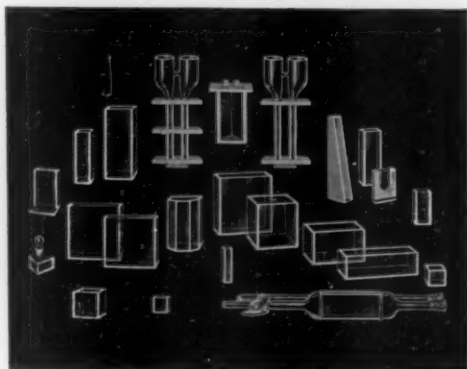
■ Kansas Academy of Science: pres., H. S. Chogguill, Fort Hays Kansas State College; pres. elect, W. H. Horr, University of Kansas; v. pres., T. F. Andrews, Kansas State Teachers College; sec., C. T. Rogerson, Kansas State College; treas., Standlee Dalton, Fort Hays Kansas State College.

■ Louisiana Academy of Sciences and the New Orleans Academy of Sciences: pres., Timothy L. Duggan, department of biological sciences, Loyola University; v. pres., Leon Segal, Southern Regional Experimental Station; sec., Arthur Welden, department of biology, Newcomb College; treas., H. B. Mouton, Bridgedale Day School.

■ North Dakota Academy of Science: pres., W. E. Cornatzer, University of North Dakota; pres. elect, W. Whitman, North Dakota Agricultural College; sec.-treas., Ben Gustafson, University of North Dakota.

■ Hawaiian Academy of Science: pres., Albert J. Mangelsdorf, Hawaiian Sugar Planters' Association, Honolulu; pres. elect, Andrew W. Lind, University of Hawaii; sec., Doak C. Cox, Hawaiian Sugar Planters' Association; treas., Beatrice Krauss, Pineapple Research Institute. Representative to the AAAS Council is Leroy D. Christenson.

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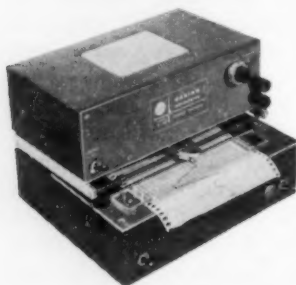
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## Forthcoming Events

### June

25-27. Health Physics Soc., Ann Arbor, Mich. (J. V. Nehemias, Univ. of Michigan, Ann Arbor.)

25-29. Ship Behavior at Sea, seminar, Hoboken, N.J. (Experimental Towing Tank Laboratory, Stevens Inst. of Technology, 711 Hudson St., Hoboken.)

25-30. International Assoc. for Bridge and Structural Engineering, 5th cong., Lisbon, Portugal. (M. L. Gretner, Swiss Federal Inst. of Technology, Zurich, Switzerland.)

26-28. Entomological Soc. of America, Pacific Branch, Berkeley, Calif. (L. M. Smith, Dept. of Entomology, Univ. of California, Davis.)

26-29. American Home Economics Assoc., annual, Washington, D.C. (Miss M. Horton, AHEA, 1600 20 St., NW, Washington 9.)

28-1. International Scientific Conf. of Rheumatism, Aix-les-Bains, France. (M. Graber-Duvernay, 6, rue de Liege, Aix-les-Bains.)

28-1. Symposium on Comparative Biology of Aquatic Species, Roscoff, Brittany, France. (G. Montalenti, Instituto di Genetica, Naples, Italy.)

### July

1-7. International Conf. on Nuclear Reactions, Amsterdam, Netherlands. (S. A. Wouthuysen, Zeeman Laboratorium, Pl. Muidergracht 4, Amsterdam (C).)

1-7. National Education Assoc., Portland, Oreg. (W. G. Carr, NEA, 1201 16 St., NW, Washington, D.C.)

2. Astronomical League, Miami, Fla. (W. A. Cherup, 4 Klopfer St., Millvale, Pittsburgh 9, Pa.)

2. Gamma Sigma Delta Biennial Conclave, Ames, Iowa. (J. A. Johnson, Dept. of Flour and Feed Milling Industry, Kansas State College, Manhattan.)

2-3. National Science Teachers Assoc., Corvallis, Oreg. (R. H. Carleton, NSTA, 1201 16 St., NW, Washington 6.)

2-7. Brazilian Soc. for the Progress of Science, 8th annual, Ouro Preto, Minas Gerais. (Sociedade Brasileira para o Progresso da Ciencia, Caixa Postal 2926, São Paulo, Brazil.)

6-14. International Union of Forestry Research Organizations, 12th cong., Oxford, England. (Secretariat of Union, Viale delle Terme di Caracalla, Rome, Italy.)

9-11. Symposium on Chemical Additives in Foods, 2nd of 5 symposiums, Amsterdam, Netherlands. (H. F. DuPont, International Bureau of Analytical Chemistry, 18 Ave. de Villars, Paris 7.)

11-14. American Malacological Union, annual, San Diego, Calif. (Mrs. M. C. Teskey, P.O. Box 238, Marinette, Wis.)

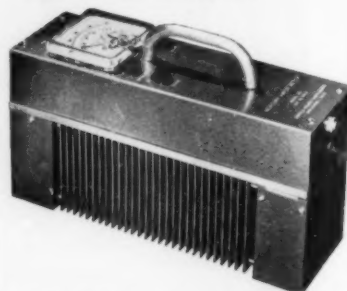
12-14. International Astrophysical Symposium on Molecules in Cosmic Sources, 7th, Liege, Belgium. (H. C. Urey, Inst. for Nuclear Studies, Univ. of Chicago, Chicago 37, Ill.)

16-17. Symposium on Synthetic Polymer Chemistry, Notre Dame, Ind. (G. F. D'Alelio, Dept. of Chemistry, Univ. of Notre Dame, Notre Dame.)

16-21. French Assoc. for the Advance-

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ment of Science, Dijon, France. (Mlle. Henri-Martin, Secretary, 28, rue Serpente, Paris 6°.)

17-26. International Soc. of Photogrammetry, 8th cong., Stockholm, Sweden. (P. O. Fagerholm, Bragevägen 8, Stockholm.)

18-20. Soc. for the Study of Development and Growth, annual, Providence, R.I. (M. V. Edds, Jr., Brown Univ., Providence 12.)

22-27. International Cong. of Pediatrics, 8th, Copenhagen, Denmark. (Prof. Franconi, Kinderspital, Steinwiesstrasse 75, Zürich 32, Switzerland.)

22-28. International Cong. on Housing and Town Planning, Vienna, Austria. (H. van der Weijde, International Federation for Housing and Town Planning, Paleisstraat 5, The Hague, Netherlands.)

22-28. International Cong. of Radiology, 8th, Mexico, D.F., Mexico. (J. Noriega, Tepic 126, 2° piso, Mexico, D.F.)

23-26. International Cong. of Developmental Biology, 1st, Providence, R.I. (J. W. Wilson, Dept. of Biology, Brown Univ., Providence.)

25-27. Conf. on Solar-Weather Relationships sponsored by American Meteorological Soc., Boulder, Colo. (K. C. Spengler, 3 Joy St., Boston 8, Mass.)

26-28. International Conf. on Biochemical Problems of Lipids, 3rd, Brussels, Belgium. (R. Ruyssen, St. Jansvest 12, Univ. of Ghent, Ghent, Belgium.)

27-31. Symposium on Cyto differentiation (invitation), Providence, R.I. (J. W. Wilson, Dept. of Biology, Brown Univ., Providence.)

27-7. International Limnology Cong., 13th, Helsinki, Finland. (H. Luther, Snellmangatan 16 C 36, Helsinki.)

30-4. International Physiological Cong., 20th, Brussels, Belgium. (J. J. Reuse, Faculté de Medecine, 115 Boulevard de Waterloo, Brussels.)

## August

1-6. International Cong. of Human Genetics, 1st, Copenhagen, Denmark. (Secretariate, 1st ICHG, 14, Tagensvej, Copenhagen, N.)

5-10. International Conf. of Social Work, 8th, Munich, Germany. (J. R. Hoffer, 345 E. 46 St., New York 17.)

6-10. Poultry Science Assoc., annual, Raleigh, N.C. (C. B. Ryan, Dept. of Poultry Husbandry, Texas A & M College, College Station.)

6-11. International Mathematical Symposium on Algebraic Topology and Its Applications, Mexico City, Mexico. (Miss J. Silva, Instituto de Matemáticas, Torre de Ciencias, Ciudad Universitaria, México 20, D.F.)

9-18. International Geographical Cong., 18th, Rio de Janeiro, Brazil. (H. O.R. Sternberg, Centro de Pesquisas de Geografia do Brasil, Faculdade Nacional de Filosofia, Av. Presidente Antonio Carlos 40, Rio de Janeiro.)

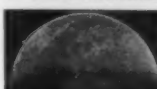
15-22. Canadian Teachers' Federation, Fredericton, N.B., Canada. (G. G. Crocker, 444 MacLaren St., Ottawa, Ont.)

16-21. Symposium on X-Ray Microscopy and Microradiography, Cambridge, England. (W. C. Nixon, Cavendish Lab., Cambridge.)

(See issue of 18 May for comprehensive list)

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## Equipment News

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is filtered into any of the octave bands from 75 to 19,000 cy/sec. Noise peaks in each of these bands can then be measured individually. For finer analysis, by frequencies within the octave bands, continuously variable filters are utilized. (Mine Safety Appliances Co., Dept. Sci., 201 N. Braddock Ave., Pittsburgh, Pa.)

■ **REFRACTORY MOLYBDENUM BORIDES** are described in a recently issued six-page bulletin that gives applications; chemical, physical, and mechanical properties; and preparations of molybdenum boride compounds. Data are given for four molybdenum borides and seven multi-boride systems. The latter include com-

positions of molybdenum borides with borides of nickel, chromium, cobalt, iron, titanium, tungsten, and zirconium. Outstanding properties of these materials are high melting points, high hardness, resistance to corrosion and abrasion, and high electric conductivity. Present and potential applications of the compounds include their use in machine parts that are subject to abrasion and corrosion and in rocket parts. (Climax Molybdenum Co., Dept. Sci., 500 Fifth Ave., New York 36.)

■ **OPTICAL WEDGE FILTERS** showing linear characteristics over a wide spectral range are available from Axler Associates. Filters can be produced to cover the spectral range of 0.240 to 2.7  $\mu$  in increments of 0.100 to 0.300  $\mu$ . They are available in sizes ranging from 1½ in. by 3 in. to 2 in. by 6 in. Peak transmissions and half widths are within the tolerance of the standard 2-by-2-in. ultraviolet, visible, and infrared transmission filters. (Axler Associates, Dept. Sci., 102 43 Ave., Corona 68, N.Y.)

■ **FERNBACH FLASKS** have been designed for use in the microbiological assay of vitamins. Made of borosilicate glass, they are provided in 5-, 10-, and 25-ml sizes. (Kimble Glass Co., Dept. Sci., Ohio Bank Bldg., Toledo, Ohio)

■ **ENZYMES** composed of glucose oxidase and catalase is described in a bulletin recently issued by Fermco Chemicals. The report discusses the effect of changes in temperature, concentration, and pH on the system in use as a soft-drink stabilizer. (Fermco Chemicals, Inc., Dept. Sci., 4941 S. Racine Ave., Chicago 9, Ill.)

■ **VAN SLYKE APPARATUS** for more accurate blood-gas analyses has been designed. Modified mechanical construction enables the new unit to operate with less vibration than former models. Readings of the etched graduation on the mercury column are facilitated by a 24-in. fluorescent tube that provides an illuminated white background for the column. Speeds of up to 400 cy/min are possible. (Central Scientific Co., Dept. Sci., 1700 Irving Park Rd., Chicago, Ill.)

■ **CHEMICALS** that are commercially available are listed and described in a 370-page book compiled by Fisher. The book includes 7300 compounds, from technical grades to radioactive reagents and spectroscopically pure solvents, along with bacteriological culture media, fluid extracts, spirits, and tinctures. The reference book gives structural formulas, formula weights, melting and boiling points, and color-index numbers of the compounds. (Fisher Scientific Co., Dept. Sci., 415 Forbes St., Pittsburgh 19, Pa.)

**1956**

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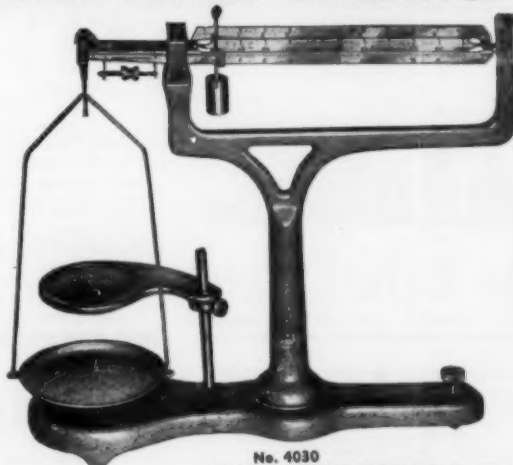
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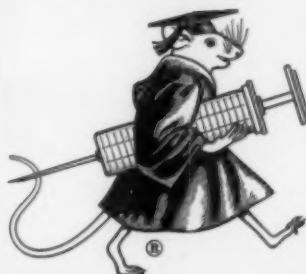
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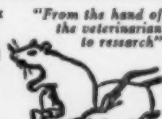
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# ANTIMETABOLITES AND CANCER

Edited by: Cornelius P. Rhoads, Sloan-Kettering Institute for Cancer Research,  
Cornell University Medical College

A Symposium Volume of the American Association  
for the Advancement of Science

6 x 9 inches, 318 pages, 54 illustrations, clothbound, 1955

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Experiments with antagonists of polio acid and observations on the mechanism of action of the sulfonamides led the way to an understanding of the significance of antimetabolite action in the control of cancer. Subsequent work has suggested that the principles involved may be found in the future to have an even more important bearing on the cancer problem than is now believed to be the case. The antimetabolite principle may also turn out to be an important implement for definition of the biochemical changes inherent in the neoplastic process, knowledge of value in establishing effective therapeutic measures.

This pioneering volume reports experimental work on plants, microorganisms, animals and man with telling development of basic underlying principles.

## (Table of Contents)

### Metabolic Fuels of the Cancer Cell

S. WEINHOUSE, The Lankenau Hospital Research Institute, and The Institute for Cancer Research

### Competitive Inhibition of Microbial Growth by Normal Metabolites

B. D. DAVIS, New York University College of Medicine

### Antimetabolites in Study of Biochemistry of Purines and Pyrimidines

E. M. LANSFORD, JR., and W. SHIVE, The University of Texas and The Clayton Foundation for Research

### Antimetabolites of Nucleic Acid Precursors

D. W. VISSER, University of Southern California School of Medicine

### Metabolic Requirements for Formation of Citrovorum Factor and Studies of Mechanism of Resistance to A-Methopterin

C. A. NICHOL and A. D. WELCH, Yale University School of Medicine

### The Seeing Eye in Science

C. P. RHOADS, Sloan-Kettering Institute for Cancer Research, Cornell University Medical College

### Mammalian Fetal Development and Antimetabolites

MAJORIE M. NELSON, University of California at Berkeley

### Effects of Antigrowth Substances in Normal and Atypical Plant Growth

LOUIS G. NICKELL, Chas. Pfizer & Co.,

### Antimetabolite Studies on Bone Marrow *in Vitro*

JOHN R. TOTTER, Oak Ridge National Laboratory

### Obliteration of Spontaneous Cancers through Discovery and Application of Some Fundamentals about Antimetabolites

D. W. WOOLLEY, The Rockefeller Institute for Medical Research

### Antimetabolite Studies in *Tetrahymena* and Tumors

ROBERT E. PARKS, JR., University of Wisconsin

### Some Aspects of the Metabolism of 8-Azaguanine

H. GEORGE MANDEL, The George Washington University School of Medicine

### Mechanism of Drug Resistance to Metabolite Antagonists in Neoplastic Cells

HOWARD E. SKIPPER, Southern Research Institute

### Studies on Analogs of Purines and Pyrimidines

GEORGE H. HITCHINGS, The Wellcome Research Laboratories

### Tumor-Destroying Effects of Viruses

DAVID R. GINDER, Emory University School of Medicine

### Antimetabolite Principle as Applied to Hormone-Induced Tissue Growth and to Hormonal Control of Neoplasms

ROY HERTZ, National Cancer Institute

### Antimetabolite Treatment of Leukemia

JOSEPH H. BURCHENAL, Sloan-Kettering Institute for Cancer Research and Memorial Center for Cancer and Allied Diseases

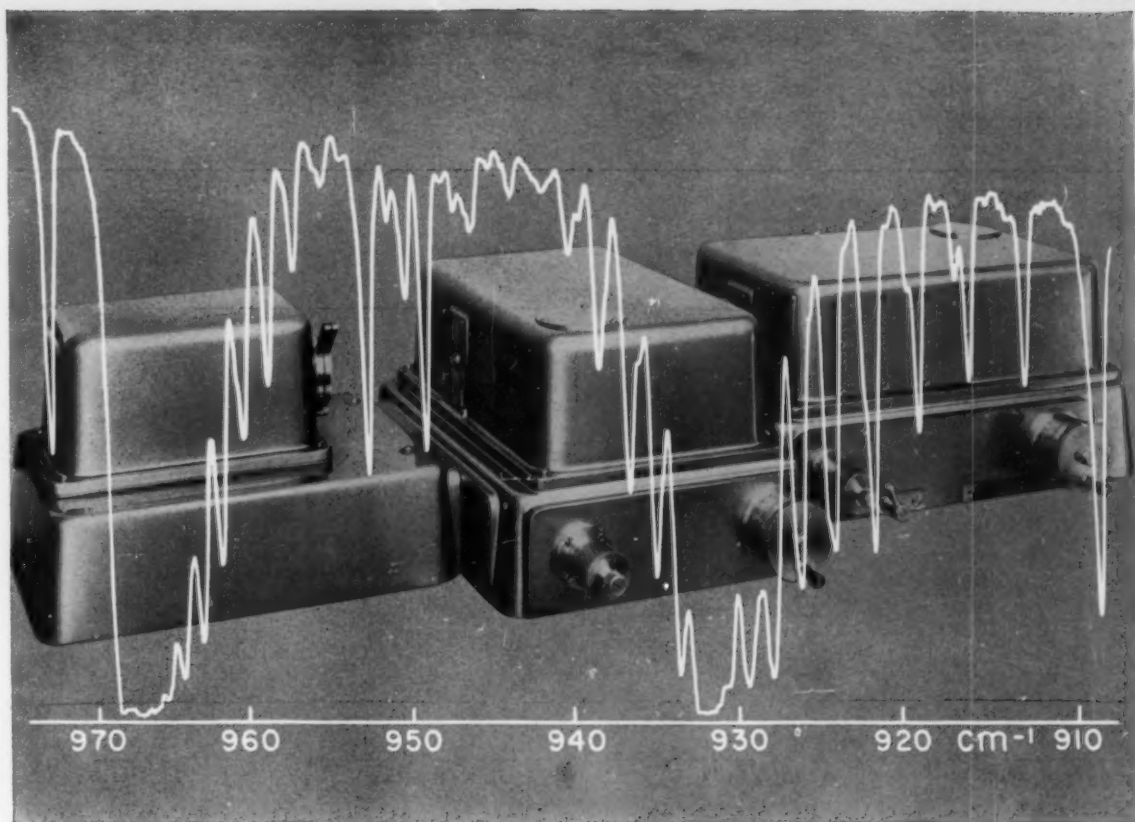
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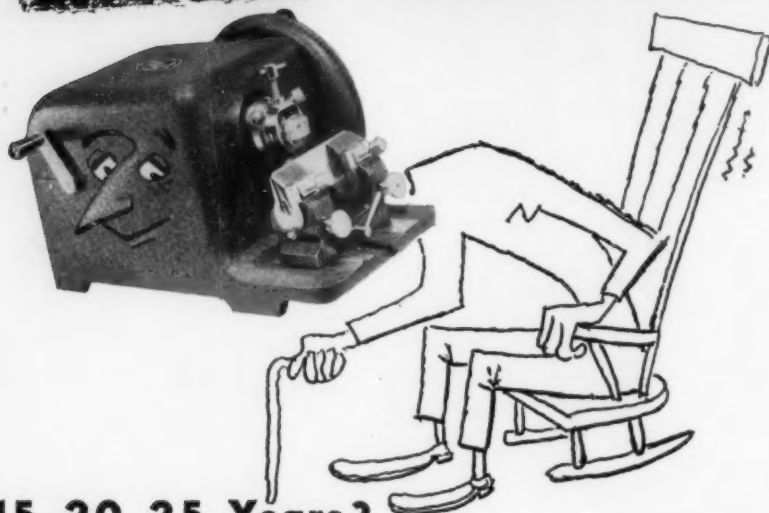
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